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Engineering Advances:
New Opportunities for Biomedical Engineers

IEEE Engineering in Medicine and Biology Society
16th Annual International Conference
November 3-6, 1994
Baltimore, Maryland

SYMPOSIUM
ON
MEDICAL DUAL-USE TECHNOLOGIES

PROGRAM

Organizers: Donald P. Jenkins,
Nicholas DeClaris*
Nicholas Diakides**

The goals of this symposium are (i) to assess the current and future potential of a number of key technology areas of special interests to ARPA and to biomedical engineers and educators, and (ii) to define the directions of future research in these interdisciplinary areas. Invited experts will summarize recent developments in their research area. Panel discussions, with audience participation, will focus on the challenges and benefits in advancing the technologies.

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***the University of Maryland, Medical Informatics Laboratory, and**
**** the Army Research Office, Washington, D.C.**

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SESSION 1
*ADVANCED DIAGNOSTICS AND DIAGNOSTIC IMAGERY
FRIDAY NOVEMBER 4

10:30 am to 12:00 pm, Pratt Room

Non-Invasive Biosensors on the Combat Casualty: The Case for MEMS and Low-Power Electronics.

Steven Jacobsen, Ph.D.
Center for Engineering Design
University of Utah
Salt Lake City, Utah

Advanced Diagnostic Imagery: Portable, Trauma-Care Focus

Francis W. Patten, Ph.D.
ARPA/Defense Sciences Office
Arlington, Virginia

Advanced Diagnostic and War Theater Telemedicine Infrastructure

Donald P. Jenkins, Ph.D.
ARPA/Defense Science Office
Arlington, Virginia

Panel Discussion with audience participation: Panel Members 20 minutes
Audience Participation 30 minutes
Moderator: Dr. Donald Jenkins

REMARKS:

SESSION 2
•MEDICAL AND SURGICAL INTERVENTION
FRIDAY NOVEMBER 4

1:30 to 3:00 pm, Pratt Room

Remote Telepresense Surgery

Richard M. Satava, M.D., Colonel, USA
ARPA/Defense Sciences Office
Arlington, Virginia

Life Support of the Critically Injured Casuality in Remote Settings

William Weisman, M.D., Colonel, USA
Division of Surgery, Walter Reed Institute of Research
USA Medical Research & Material Command
Washington, D.C.

Medical and Surgical Management of Trauma Patients

Howard R. Champion, M.D.
Department of Surgery, Uniformed Services University of the Health Sciences
Bethesda, Maryland

Panel Discussion with audience participation: Panel Members 20 minutes
Audience Participation 30 minutes
Moderator: Dr. Richard M. Satava

REMARKS:

SESSION 3
•MEDICAL INFORMATICS AND INFORMATION INFRASTRUCTURE
FRIDAY NOVEMBER 4

4:30 to 6:00 pm, Pratt Room

Scenario-Based Engineering for the National Health Information Infrastructure

Karan Harbison, Ph.D.
Department of Computer Science
University of Texas/Arlington

Health Care and the National Information Infrastructure

John S. Silva, M.D., Colonel, USAF
ARPA/Software & Intelligent Systems Technology Office
Arlington, Virginia

Knowledge Based Engineering in Medicine and Health Care

Nicholas DeClaris, Sc.D.
Departments of Pathology, Epidemiology and Preventive Medicine, UMAB
Department of Electrical Engineering and Applied Mathematics, Grad. Prog., UMCP
University of Maryland

Panel Discussion with audience participation: Panel Members 20 minutes
Audience Participation 30 minutes
Moderator: Dr. John S. Silva

REMARKS:

SESSION 4
*MEDICAL SIMULATION
SATURDAY NOVEMBER 5

8:30 to 12:00 pm, Pratt Room

The Visable Human: The Basis for Surgical Simulation

Victor M. Spitzer, Ph.D.
Departments of Radiology and Cellular & Structural Biology
University of Colorado School of Medicine
Denver, Colorado

Surgical Simulation for Limb Trauma Management

Thomas S. Buchanan, Ph.D.
Rehabilitation Institute of Chicago
Chicago, Illinois

Simulation of Abdominal Viscera

Dwight A. Meglan, Ph.D.
High Techsplanations, Inc.
Bethesda, Maryland

A Virtual Design Tool for a Surgical Room of the Future

Kenneth L. Kaplan, Ph.D.
Departments of Architecture MIT, Research Lab Electronics MIT
Massachusetts Institute of Technology
Boston, Massachusetts

Panel Discussion with audience participation: Panel Members 30 minutes
Audience Participation 30 minutes
Moderator: Dr. Victor M. Spitzer
Coffee Break: 10:00 am

REMARKS:

SESSION 5
**MEDICAL INFRARED IMAGING
SATURDAY NOVEMBER 5

1:30 am to 6:00 pm, Pratt Room

Co-chairs: Dr. Raymond Balcerak, Microelectronics Technology Office, ARPA

Alfred Pavot, M.D., Greater Southern Community Hospital & Georgetown University Medical Center

Thermology in the 21st Century - the Biomedical Future of a Technology Based on Defense Oriented Engineering

Michael Anbar, Ph.D.,School of Medicine and Biological Sciences, SUNY, Buffalo

Advanced Infrared FPA for Uncooled High Resolution Systems

James Gilpin, Rockwell International, Anaheim, California

High Performance, Low Cost Uncooled IR Cameras

Bill Stearns, Texas Instruments, Dallas, TX

Quantitative Thermal Imaging in Rheumatology

Prof. Francis Ring, Royal National Hospital for Rheumatic Diseases, Bath, U.K.

Clinical Infrared Thermal Image Testing: a Noninvasive Expressions of Invisible Physiological Functions

Prof. Iwao Fujimasa, M.D., Ph.D., University of Tokyo

Pre- and Postoperative Digital Infrared Thermographic Imaging in Lumbar Disc Hermitations

Prof. Young-Soo Kim, M.D. DmSc., Yonsei University, College of Medicine, Seoul, Korea

Pre- and Postoperative Digital Infrared Thermographic Imaging in Essential Palmar Hyperhidrosis

Prof. Young-Soo Kim, M.D. DmSc., Yonsei University, College of Medicine, Seoul, Korea

The Role of Thermography in the Diagnosis and Treatment of Breast Cancer

Robert Elliott, M.D., Ph.D., Fen Wang, M.D., Michael W. Haley, M.D., and Jonathan Head, The Elliott Mastology Center, Baton Rouge, LA

Panel Discussion with audience participation.

REMARKS:

Engineering Advances:
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SYMPOSIUM ON

MEDICAL DUAL-USE TECHNOLOGIES

Organizers:

Donald P. Jenkins,
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Nicholas Diakides**

SESSION VI: MEDICAL INFRARED IMAGING

The goals of this symposium are (i) to assess the current and future potential of a number of key technology areas of special interests to ARPA and to biomedical engineers and educators, and (ii) to define the directions of future research in these interdisciplinary areas. Invited experts will summarize recent developments in their research area. Panel discussions, with audience participation, will focus on the challenges and benefits in advancing the technologies.

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Baltimore, Maryland

SYMPOSIUM on MEDICAL DUAL-USE TECHNOLOGIES
SESSION 6: MEDICAL INFRARED IMAGING

Saturday, November 5, 1:30 - 4:30, Pratt Room

Co-chairs: Raymond Balcerak, Microelectronics Technology, ARPA
Alfred Pavot, M.D., Georgetown Univ. Medical Center

1:30 - 1:50 **Thermology in the 21st Century - the Biomedical Future of a Technology Based on Defense Oriented Engineering.** Michael Anbar, Ph.D., School of Medicine and Biological Sciences, SUNY, Buffalo.

1:50 - 2:10 **The Role of Thermography in the Diagnosis and Treatment of Breast Cancer.** Robert Elliott, M.D., Ph.D., Fen Wang, M.D., Michael W. Haley, M.D., and Jonathan Head, Ph.D., The Elliott Mastology Center, Baton Rouge, LA.

2:10 - 2:30 **Pre- and Postoperative Digital Infrared Thermographic Imaging in Lumbar Disc Herniations.** Young-Soo Kim, M.D., DMSc., Yonsei University College of Medicine, Seoul, KOREA

2:30 - 2:50 **Quantitative Thermal Imaging in Rheumatology.** Francis Ring, D.Sc., Royal National Hospital of Rheumatic Diseases, Bath, U.K.

2:50 - 3:10 **Clinical Infrared Thermal Image Testing: a Non-invasive Expression of Invisible Physiological Functions.** Iwao Fujimasa, M.D., Ph.D., University of Tokyo, JAPAN

3:10 - 3.30 **Low Cost Uncooled Thermal Imaging.** Charles Hanson and Bill Stearns, Texas Instruments, Dallas, TX.

3:30 - 3:50 **Rockwell's Low Cost, High Resolution IR Sensors Make IR Imaging Available to the Medical Community.** James Gilpin, Rockwell International, Anaheim, CA.

3:50 - 4:10 **The Clinical Utility of Thermology.** Gerald S. Goldberg, M.D., Pain Care Center, Plantation, FL.

4:10 - 4:25 Panel Discussion (Questions and Answers).

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Thermology in the 21st Century - the Biomedical Future of a Technology Based on Defense Oriented Engineering

Michael Anbar Ph.D.

School of Medicine and Biomedical Sciences, SUNY, Buffalo

The development of clinical applications based on infrared telethermometry of human skin has been slower than anticipated from a risk free, inexpensive technique that is applicable to a very large variety of clinical situations. In addition to expected antagonism from older technologies, there are three major reasons for this. First, in spite of offering quantitative information, most thermological tests have remained qualitative and subjective. Second, it has not been fully realized that abnormal thermal behavior, depicted in thermal imaging, often represents a physiological rather than an anatomical dysfunction. Most of the diagnostic information exists, therefore, in the time domain, rather than in the spatial distribution of temperature. A dynamic approach is needed, therefore, to study thermoregulatory dysfunction. Third, relatively little attention was given to mechanisms of physiological dysfunctions that manifest thermal abnormalities. Once these shortcomings are realized, thermological testing can be substantially improved by optimizing the testing conditions, including the hardware and software used.

These points are illustrated by examining the case of breast cancer hyperthermia. It is concluded that breast-cancer-induced hyperthermia involves a thermoregulatory dysfunction rather than hypermetabolism or hypervascularization. Consequently, breast cancer induced hyperthermia is expected to be associated with a characteristic dynamic thermal behavior. To make them more sensitive and specific, screening tests for breast cancer must be substantially changed, including the equipment, the software and the interpretation of the thermal data.

Following the same rationale, quantitative and dynamic telethermometry is expected to be extensively used in the diagnosis and management of diabetes mellitus, liver disease, arthritis, dermatology, neonatology, and neurological disorders, all of which involve thermoregulatory dysfunctions, in addition to open heart surgery, kidney transplant, vascular and reconstructive surgery, where telethermometry provides real time information on perfusion or reperfusion.

Key words:

Thermography, thermology, thermoregulatory dysfunction, dynamic area telethermometry, DAT, breast cancer, hyperthermia, perfusion, immune response, diabetes mellitus.

Introduction

Thermal images of the human skin contain a tremendous amount of clinical information that can help to diagnose numerous pathological conditions ranging from cancer to emotional disorders, from endocrine or metabolic illness to autoimmune diseases, from neurological dysfunctions to skin infections, and from neonatology to ophthalmology. With the possible exception of X-ray radiology there is hardly any other diagnostic technique with as wide a range of clinical applications. However, unlike radiology, telethermometry is an utterly harmless, non-invasive and inexpensive technique that quantitatively measures spatial and temporal abnormalities in blood perfusion of skin. Thermal imaging is the only known technique that can measure skin perfusion simultaneously over large areas. It can reflect, therefore, a variety of physiological and anatomical parameters. The instrumentation needed for area telethermometry of the skin is readily available; it is based on the sophisticated modern infrared technology that was originally developed for military purposes. Yet telethermometry has not been accepted by the medical community, at least in the United States, as a valid diagnostic technique. In this paper we will try to review the history of use of this medical technology and understand the reasons for its limited progress. We will then discuss means to overcome the historical technological and conceptual shortcomings, and project the role of this powerful technique in future health care.

Historical Overview

From the dawn of medicine in times long forgotten, body temperature has been used as a tool to assess the condition of sick people. Observation of abnormal temperature on any part of the body indicated ailment long before natural causes of different diseases were discovered. Already twenty five hundred years ago, the importance of ***thermoregulation*** in human health was conceptualized by the Greek philosophers. However, it is less than 500 years ago that man invented the thermometer, an instrument that ***measures*** temperature ***quantitatively***. The clinical thermometer, which measures temperature only at a single spot and requires a relatively long equilibration time, allowed ***objective*** assessment of acute disease and a reliable follow up of recovery. The classical, liquid-filled thermometer was probably the first quantitative clinical instrument that ushered the era of modern medical diagnostic technology. Although it has been known for a very long time that additional diagnostic information could be derived from abnormal ***surface*** temperature of the forehead, the hands, feet, or other areas all over the human body, only the last fifty years produced tools to ***quantitatively*** measure abnormalities in ***skin*** temperature. But measurement of skin temperature is generally diagnostically meaningless unless done ***simultaneously*** at ***many*** spots; this cannot be done by classical single spot thermometry. In other words, medical diagnosis based on abnormal thermal behavior of the skin had to await the availability of ***area thermometry***.[1]

Area thermometry can follow two approaches - contact area thermometry and non-contact thermometry (***telethermometry***). Contact thermometry (using thermocouples, thermistors, or liquid crystals) has severe limitations as a clinical diagnostic technique. These include low spatial thermal resolution and long equilibration time. Moreover, stimulation of the innervation of the measured skin on contact may result in significant artifactual temperature changes. These changes may either conceal or accentuate pathological thermal behavior and thus lower the sensitivity or specificity of diagnostic tests.

Fortunately, in parallel with the development of contact area thermometry, the defense industry has developed cameras that measure infrared emission above 3 μm to meet a number of different military needs, including night vision for field use, airplane and satellite surveillance, and missile guidance systems. Area telethermometry of skin, based on the blackbody emission in the 8 to 14 μm region, is best achieved by appropriate infrared cameras. Most modern infrared cameras systems were developed with a computer interface to allow surveillance and pattern recognition. Such computer interface can translate infrared emission values into temperatures readings of each spot (pixel), and thus generate a ***thermal image***. This allows ***quantitative*** assessment of skin temperature ***distribution*** over areas of interest with a precision of better than 0.01°C and a high spatial resolution (e.g., 0.1 mm at a distance of 50 cm between the camera and the observed area). In other words, technology, originally developed for defense purposes, has provided medicine with the tools needed for ***quantitative*** assessment of skin temperature distribution. Moreover, ***fast responding*** military infrared cameras, that must meet the needs of air born surveillance and rapidly moving homing devices, offer medicine a tool to measure ***temporal*** changes in temperature distribution and thus study the ***dynamics*** of ***thermoregulation***.

The availability of ***thermal imaging*** -- the presentation of the spatial distribution of temperature over a given area -- has begun the history of using skin temperature as a clinical diagnostic tool. In parallel with X-ray ***radiography*** there emerged a clinical imaging modality named "***thermography,***" based on thermal imaging. (Thermography should not be confused with ***thermology***, the science of biological thermal ***behavior***, which can use different thermometric techniques in ***quantitative*** studies; ***clinical thermology*** applies this behavior in clinical settings). In the beginning, as soon as area thermometry became available, thermal imaging was explored in many different fields of medicine essentially in a purely ***empirical*** manner, wherever changes in skin temperature were observed under pathological conditions. When a diagnostic test was proposed, based on an observed abnormality in skin temperature, the immediate goal was generally to establish its ***sensitivity*** and ***specificity*** to make the test credible. However, this goal was rarely achieved, mostly because relatively little consideration has been given to the ***mechanism*** that causes the observed pathological change in skin temperature. The mechanism of thermal abnormalities might be (i) anatomical - mechanical or (ii) physiological - functional. Failure to make this distinction has resulted in inconsistent and inconclusive clinical studies. Many early users of "thermography", especially those with prior training as radiologists, used a purely anatomical approach to interpret "thermograms", relating them to X-ray radiograms and ended up utterly frustrated. Some of these disappointed radiologists have become sworn enemies of thermal imaging and have contributed to the negative attitude toward clinical thermology prevailing in medicine up to date.

While anatomical factors (vascular malformations or occlusions) may result in abnormal skin perfusion and consequent thermal abnormalities, the majority of thermal aberrations are the result of physiological dysfunctions. These may be (a) neurological, (b) immunological, or (c) metabolic; the mechanism of an abnormality may often involve a combination of different anatomical and physiological factors, because certain dysfunctions may trigger others. Physiological manifestations are characterized by changes of skin temperature ***with time***, either spontaneously (due to regulatory processes) or under

challenge (again, due to normal or abnormal thermal homeostasis). As stated, classical "thermography" had a rather limited success because of lack of appreciation of the importance of temporal changes in skin temperature distribution. This erroneous approach also resulted in the extensive use of slow and imprecise temperature measuring devices (generally, liquid crystals), which further contributed to disappointing results.

The general interest in clinical thermological studies has been declining in recent years as can be seen from the number of published papers on thermology catalogued by the National Library of Medicine (see Figure 1). The recent decline in productive research in thermology is even greater than it appears in Figure 1, because many of the recent publications are merely critiques of older studies. This decline resulted from a combination of disappointing findings of poorly designed studies and a steep decline in third party remuneration for thermological tests.

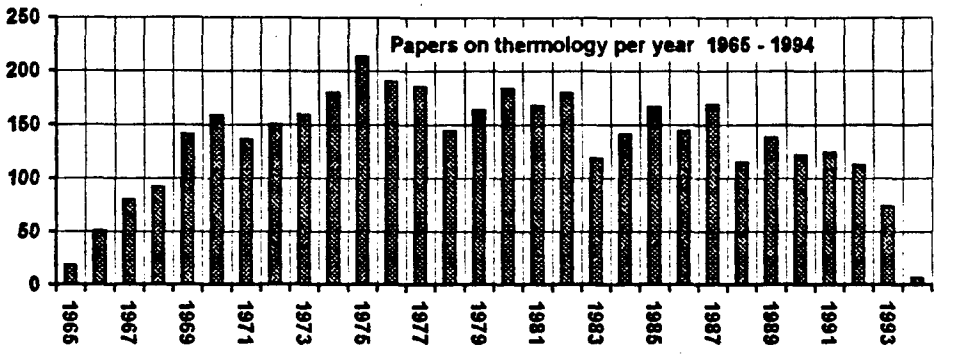

FIGURE 1. **Papers on thermology catalogued in the National Library of Medicine**

At this point in time, thermology is at a crossroad -- either it becomes strongly anchored in biomedical science as a quantitative, well documented technique that is based on well understood scientific grounds, or it may fade away, at least for some time, as an unproven idea to be rediscovered at a later date. The low stature of clinical thermology in the United States has been not just the result of hostile politics, but also of the failure to fully recognize that, at this day in age, thermology must be better rooted in biomedical ***science***. I believe that thermology can get on the right track on route to be recognized by the medical community and by makers of health care policy.

Evaluation criteria for thermological tests

By now it has been realized that, like in most other fields in medicine, the understanding of the ***mechanism*** of an observed abnormality is the key for its effective use in medical diagnosis and management. The mechanism of thermal abnormality can be understood only after the following critical questions have been answered:

(1) What is the ***temporal*** behavior of the observed abnormality? Is it permanent or transient, and if it is transient, what is the rate of the temperature modulation? Is it periodic, and if so what is its periodicity?
(2) Is the abnormal thermal behavior of skin ***local***, ***regional*** or ***systemic***?
(3) Can it be accentuated or alleviated, and if so, what might cause such an effect?
(4) What is the quantitative ***correlation*** between the thermal dysfunction and the severity of the underlying pathophysiological process, and how is that pathophysiology related to the severity of the symptoms?
(5) What is the ***mechanism*** of the underlying pathophysiology?

In most cases where thermological diagnostic procedures were advocated, these questions have not yet been answered. In many cases they were not even asked. This is a major reason for the lack of progress in the use of thermal imaging as a diagnostic technique.

Further, to evaluate a given thermological dysfunction in a routine diagnostic test, one must include answers to the following questions:

(1) What ***other*** pathophysiological changes are associated with the given abnormality in skin temperature and what is the causal relationship between them?
(2) Can those associated dysfunctions be detected ***easier*** by alternative techniques? If so, what is the point of promoting thermology for that particular clinical niche?

(3) Since different thermological tests require different telethermometric instruments, what is the most cost effective instrumentation to detect or measure the given dysfunction?
4) What is the ***primary*** objective of a proposed thermological test – is it a ***screening*** test, a ***preliminary*** diagnostic test, or a ***confirmatory*** test? Should it be used to ***stage*** a condition that was diagnosed by other means, or is its primary goal to determine the efficacy of a given treatment?
(5) What will be the effect of a given thermological test on the ***clinical outcome*** of individual patients?
(6) What will be the effect of the routine use of a given thermological test on the efficacy of health care at large?

Failure to take into consideration all these questions, has led to suboptimal use of the technology and to repeated failures of attempts to convince clinicians to use skin temperature imaging as a valid clinical tool. It is necessary to explain exactly what ***biomedical parameter*** is being tested and what is the explicit ***purpose*** of a test, before one tries to run clinical tests on hundreds of patients in order to determine its sensitivity or specificity.

Applying the cited criteria to a case study – the screening for breast cancer

There is hardly a topic in thermology that has been more controversial than the use of thermal imaging in the diagnosis or management of breast cancer.[1] Nobody disputes that a strong association exists between breasts malignancy and abnormal thermal behavior of the breast, yet this thermal abnormality did not become the basis of a reliable diagnostic test. More than one thousand research papers, chapters and abstracts were published to date on this subject alone. Of these, more than eight hundred papers can be retrieved from the electronic files of the National Library of Medicine for the 27-year period of 1966 through 1993 (see Figure 2). Most of these papers appeared before 1984 when several clinical studies, including a National Cancer Institute sponsored multicenter study, concluded in 1979 that thermography (as used in those days!) lacks the sensitivity and specificity to compete with X-ray mammography. Telethermometry has substantially improved in the past 15 years. On the other hand, also ***up-to-date*** X-ray mammography does not always differentiate between malignant and benign lesions, and even with modern radiological equipment the current sensitivity of X-ray mammography is still below 85%,[2-5] (below 92% for palpable! breast tumors).[6] The greatest difficulty in X-ray mammography is posed by dense breasts, which constitute 25% of the tested population.[7] It is worthwhile, therefore, to reexamine the possible use of thermal imaging as an alternative screening test, based on the two sets of generic criteria outlined above.

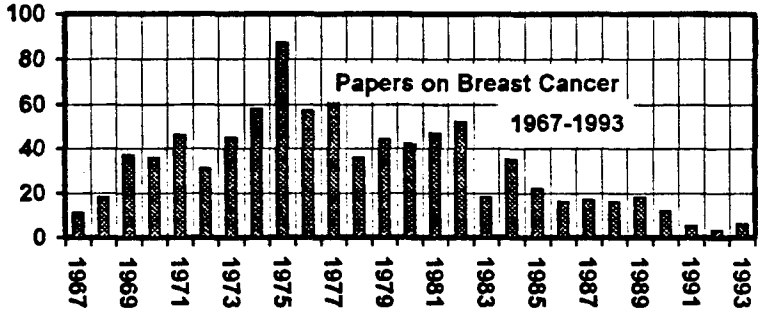

FIGURE 2. **Papers on breast cancer catalogued in the National Library of Medicine**

To follow the order of the first set of questions listed above, little attention was given to the temporal behavior of breast hyperthermia; however, several studies have reported abnormal thermal oscillatory behavior of hyperthermic breasts compared with normal ones.[8-10] Hyperthermia of the cancerous breast is evidently local. It has been known for a long time that cooling of the two breasts by evaporating a spray, accentuates the ***relative*** hyperthermia of the affected breast,[11,12] and this effect has been used in many subsequent studies; in other words, the cancerous breast seems not to undergo vasoconstriction following a cold stimulus. It was repeatedly reported that hyperthermia is positively correlated with the virulence of the neoplastic tissue in terms of its growth rate and metastatic potential,[13-15] however, this correlation could not always be confirmed, probably because of the imprecision of a procedure that used thermal asymmetry between the two breasts as its sole criterion.[1]

As was pointed out very recently,[16] relatively little attention was paid to the mechanisms through which cancer may cause hyperthermia. These mechanisms include hypermetabolism, hypervascularization, and thermoregulatory dysfunction

(expressed in enhanced vasodilation) associated with immune response. Hypermetabolism inside the malignant tissue or associated with phagocytosis in its periphery, is not plausible on energetic grounds. Breast cancer is detected by thermal imaging with a relatively high sensitivity often using thermal asymmetry between the breasts of 1°C as threshold of significance. To maintain an elevated temperature in, say 500 ml of breast tissue by just 0.5°C, assuming a blood flow rate that exchanges the blood pool within 10 seconds, one would need a power output from the tumor of 50 cal/sec i.e., more than 2100 Kcal/24 hrs (comparable to the ***total*** caloric value of daily food intake). It must be concluded, therefore, that breast hyperthermia ***must*** be due to an enhanced flow of blood at core temperature. This enhanced blood flow cannot be due to hypervascularization associated with the malignancy. Since breast skin is about 5°C cooler than core temperature, an increase of approximately 20% in the ***average*** blood flow is needed to increase the average temperature of the breast by 1°C. If a hypervascularized small sized tumor (radius of 0.5 cm) was responsible for raising the temperature of an area of say, 100 cm^2 by 1°C, its internal blood flow would have had to increase by a factor of 12!. In brief, in spite of the fact that cancerous tissue is often hypervascularized, this does not account for the detectability of tumors by thermal imaging. Moreover, there is no relationship between angiogenesis of breast cancer and its potential to metastasize, contrary to the reported correlation between thermal detectability and that potential.[1,16]

The probable mechanism is, therefore, ***dysfunction*** of the thermoregulatory processes induced by the malignancy. This dysfunction results in enhanced blood flow ***throughout*** a large part of the affected breast. It is highly plausible that enhanced release of nitric oxide (NO) is involved in this ***regional*** vasodilation, since NO was recently found to induce vasodilation in many other tissues under a variety of conditions.[1,16-18] If substantial amounts of NO are generated by the tumor and by the macrophages associated with the immune response to it, which is plausible in view of the behavior of other cancerous conditions,[19-21] it will cause the vasodilation of the whole capillary bed of the breast, because NO diffuses freely through tissues.[1,16]

Another significant observation was that ferritin, an iron carrying cytolytic enzyme, was found at twice the concentration in breast tumors that showed significant unilateral hyperthermia, compared to its level in tumors that were defined as undetectable by this technique (showing thermal asymmetry below the threshold of significance).[14] The high local concentration of ferritin in malignant tumors may contribute to the suppression of the immune response, since high ferritin concentrations inhibit the phagocytic activity of neutrophils.[1,16]

Now, there is a noteworthy relation between NO and ferritin. Fe^{++} mobilized from ferritin promotes the formation of hydroxyl radicals. These radicals were reported to be involved in the production of nitroso arginine, the precursor of nitric oxide.[1] Also nitric oxide syntase, the enzyme responsible for synthesis of nitric oxide from arginine, requires Fe^{++} for its own synthesis. On the other hand, nitric oxide was shown to mobilize Fe^{++} from ferritin.[22,23] This means that ferritin under aerobic conditions may help to produce NO by an ***autocatalytic*** process.[16] Autocatalytic processes are characterized by an oscillatory behavior, caused by the periodic depletion of one of the precursors. The autocatalytic generation of nitric oxide implies oscillations in the level of nitric oxide produced in the affected ferritin containing tissue. It is conceivable, therefore, that a ferritin-rich tissue will produce excessive amounts of NO, which can diffuse over a relatively long range and thus contribute to regional vasodilation and subsequently result in hyperthermia.[16] This vasodilatory hyperthermic effect is expected to be oscillatory in nature, in line with the findings cited above about the abnormal temporal behavior of cancerous hyperthermia. High levels of nitric oxide inhibit sympathetic vasoconstriction and thus result in loss of sympathetic reflexive control, in line with the finding that surface cooling does not induce local vasoconstriction in the cancerous breast, as it does in the normal breast.

In brief, it is not the tumor's temperature, but its chemical messenger that causes hyperperfusion in the ***surrounding*** tissues, making them hyperthermic and detectable by telethermometry. This explains how a minuscule ***reactive*** malignant tissue situated, say, 10 mm below the skin surface, can be detected at skin level by its effect on ***local*** or ***regional*** thermoregulation. Most importantly, understanding of the mechanism of hyperthermia induced by breast cancer has an immediate practical return. Since this mechanism implies ***characteristic*** oscillations and the attenuation or abolishment of the neurological thermoregulatory frequencies,[24,25] monitoring the temporal behavior of the hyperthermic breast without external cooling offers a more specific and robust criterion of malignancy. This can be done by the use of dynamic area telethermometry (DAT), which measures the frequencies of thermoregulatory processes.[25,1] DAT does not involve subjective imaging but is a quantitative, objective technique that produces hard data of frequencies and amplitudes for any area of interest. This means that DAT requires substantially less expertise to interpret its findings than an imaging procedure. This makes DAT not only more reliable but also less costly. Furthermore, since DAT measures temperature ***modulation*** rather than temperature, it calls for minimal thermal equilibration time before measurement. This increases the

throughput of patients per camera and a corresponding lowering of cost per test. A study is now in progress to verify the adequacy of this new diagnostic methodology.

Let us now examine the DAT screening test following the second set of criteria cited above: The two other pathophysiological changes associated with breast cancer, currently used to detect it, are the palpable mass of the tumor and its rentgenologically detectable calcification. Both these manifestations are directly correlated with the size of the lesion but not directly with its proliferative or metastatic potentials. Since the latter are the critical parameters that call for ***early*** detection, DAT is the method of choice, assuming identical sensitivity and specificity for the alternative diagnostic approaches. Since X-ray mammography has currently only a small advantage over ***classical*** thermal imaging in terms of sensitivity and specificity,[1] and since DAT is expected to improve both these parameters, it is likely to be preferred over X-ray mammography not only because it is less costly and risk free, but also on grounds of testing effectiveness.

DAT requires different instrumentation than thermal imaging. DAT requires a highly stable and precise infrared camera with appropriate software and storage capacity, but, on the other hand, its spatial resolution (pixels per field of view) can be lower than used in advanced imaging systems. Although it requires 12 bit A to D conversion to assure precision of the temperature readings, it does not require storage of 16 bit pseudocolor information. In other words, optimizing performance at a minimal cost for a ***routine*** test requires a specially designed camera. This DAT test of women's breasts would be used primarily for screening and staging, however, it could also be used to follow up surgery or radiation therapy to find out the extent of elimination of the cause for enhanced immune response.

There is little doubt that earlier detection of breast cancer based on the immune response, even before calcification makes it detectable by X-ray mammography, is highly desirable both from the standpoint of the individual patient and of public health. Since the cost per DAT test is expected to be significantly lower than that of X-ray mammography, it is undoubtedly a desirable development also from the viewpoint of health care economics. In brief, DAT screening for breast cancer rates favorably according to each of the six generic criteria outlined above. It is, therefore, worthy of support for research and development, including extensive clinical studies.

Clinical thermology in the 21st Century

Looking into the future, there are three major factors in favor of thermology:

A. There is a thrust to develop ***inexpensive***, non-invasive, diagnostic tests for screening, staging and managing of disease; tests that require no special facilities, that do not pose waste disposal or other environmental problems, and that call for minimal personnel training. While such a need exists in the United States, this need is even greater in most other countries. Computerized thermal imaging combined with rudimentary pattern recognition and DAT, meet these criteria.

B. Infrared technology has been developed for other purposes far beyond the current needs of clinical thermology, thus no new specialized technology has to be developed. The fine tuning of the technology to match it with specific clinical needs is a relatively minor effort that will be undertaken by equipment manufacturers, once an appropriate market is apparent.

C. Physiological and biochemical research in the last decade have provided a good base for answering many of the scientific questions concerning function and dysfunction of thermoregulation. This has been illustrated above for breast cancer. Putting thermological findings on a firm scientific footing will make this technology acceptable even to the greatest skeptics in academic medicine.

Since both, the technology and the basic science are available, and since the number of potential clinical applications is growing, there is little doubt that the current barriers to the acceptance of thermological tests will be removed and appropriate research support will become available to implement this technology world wide.

Clinical areas that are in line to benefit from this technology include:

(1) **Open heart, vascular and organ transplant surgery**. Thermal imaging has been used successfully during surgery to monitor occlusions and reperfusion,[1] both of which are critical parameters in vascular and cardiovascular surgeries. In the case of open heart surgery, an outcome study has demonstrated the efficacy of intraoperative use of an infrared camera to monitor perfusion in real time.[26] This straight forward use of thermal imaging can also monitor ***changes*** in perfusion in real time; changes in perfusion can be displayed by subtraction of consecutive images. Similar thermological uses exist in reconstructive surgery. In the latter case, DAT can supplement real time thermal imaging by monitoring the re-establishment of nervous control.

(2) **Staging and management of diabetes mellitus**. Although thermal imaging has been used to assess perfusion of gangrenous legs in diabetics, to optimize the outcome of amputation,[1] little use has been made of a much more important

potential of this technology. In the ***staging*** of this disease and selecting the appropriate treatment strategy, it is important to differentiate early vascular dysfunction from the subsequent neuropathy. DAT, which quantitatively measures the functions of the sympathetic system, can determine the cause of diabetes-induced hypoperfusion or glucose induced enhanced perfusion.[1] DAT may thus become a routine test in the management of this common disorder.

(3) **Neonatal care and diagnosis of neurological and metabolic disorders in infants.** Preliminary studies have demonstrated the use of real time skin temperature monitoring inside incubators and its value in assessing the early stages of development of nervous control in newborns.[1] Early detection of neurological disorders such as muscular dystrophy (MS) or cerebral palsy (CP), may mitigate some of the detrimental consequences if detected at a very early stage. The latter disorder is prevalent in low birthweight babies and its early diagnosis is difficult. A simple non-contact DAT screening test, if found effective, could be performed on all newborns, or at least on all genetically prone and low birthweight individuals.

(4) **Screening for breast cancer.** This DAT test has been discussed above. If proven effective, this risk free, non-contact, inexpensive test (estimated cost <$25, including a reasonable profit for the provider)[1] could have a significant impact on health care of women.

(5) **Autoimmune joint disorders.** Most autoimmune diseases with peripheral manifestations are associated with inflammatory processes i.e., with enhanced nitric oxide production and its subsequent vasodilation and hyperthermia. Most common among these is rheumatoid arthritis. Even classical infrared imaging was shown to be very helpful in managing this disease.[27] DAT is expected to be even more effective in managing these disorders by non-invasively providing a quantitative measure of the loss of neurological control which reflects the extent of local inflammation.[1,28] This unique feature of DAT may facilitate optimized pharmacological, nutritional or physiotherapeutic treatments.

(6) **Dermatological disorders, including skin neoplastic diseases (e.g., malignant melanoma)**. Different modalities of thermology can be extremely useful in dermatology. DAT can assess allergic and other immune responses, including those to neoplasia. Measuring the microhomogeneity of skin temperature, independently assesses the level of saturation of the cutaneous capillary bed.[29] Multiplewavelength infrared cameras can characterize various skin infections, wounds and burns by their effects on emissivity and/or fluorescence of skin.[1,30] Similarly, multiplewavelength cameras can also help in following dermatological pharmacokinetics.

(7) **Staging and management of liver disease**. Chronic liver diseases affect sympathetic nervous function in a way that can be assessed by DAT.[1] Such tests can be help in assessing the degree of liver damage, which may not be fully reflected in biochemical tests. DAT can also be useful in providing quantitative feedback on the efficacy of treatment.[1]

(8) **Neurological disorders**. None of the clinical applications listed above, each of which meets the needs of millions of patients, are currently in the mainstream of clinical thermology, which focuses primarily on neurological disorders. There is no doubt that also the diagnosis of many common neurological dysfunctions could substantially improve in the foreseeable future, especially due to the availability of DAT which provides a quantitative measure of nerve driven thermoregulatory functions.

In conclusion

The list of thermological applications presented above is not exhaustive. There are additional medical specialties and clinical conditions that might benefit from thermological studies.[1] The examples cited must, however, be sufficient to persuade anyone of the wide scope of clinical applications inherent in the quantitative measurement of the distribution of skin temperature and its temporal behavior. To implement reliable thermological tests in any of the clinical fields cited, will take two to five years of well planned research, including multicenter clinical studies. A parallel, relatively smaller effort is expected on the engineering side to meet specific needs of certain applications. This is the price that must be paid to benefit from this technology, or from any other new medical technology for that matter. In view of the substantial benefits that can be derived from the use of the different modalities of thermology, it will be highly cost effective to invest private and public resources in engineering R&D, in fundamental physiological research, and in clinical studies of the various aspects of quantitative thermology. Driven by economics and by the need for improved health care, there is little doubt that thermology will be promoted to play a major role in medicine in the 21st Century.

References

[1] For references or additional information see M. Anbar, "Quantitative and dynamic telethermometry in medical diagnosis and management.", CRC Press Inc., Boca Raton, 1994.

[2] D.R. Lannin, R.P. Harris, F.H. Swanson, M.S. Edwards *et al.* "Difficulties in diagnosis of carcinoma of the breast in patients less than fifty years of age." *Surg Gynecol Obstet* 177: 457-462, 1993.

[3] J.A. Harvey, L.L. Fajardo and C.A. Innis, "Previous mammograms in patients with impalpable breast carcinoma: retrospective vs blinded interpretation." *Am J Roentgenol* 161: 1167-1172, 1993.

[4] V.W. Lee, E.J. Sax, D.B. McAneny, S. Pollack *et al.*, "A complementary role for thallium-201 scintigraphy with mammography in the diagnosis of breast cancer". *J Nucl Med* 34: 2095-2100, 1993.

[5] G.J. den Heeten, W.J. van Rooij and J.A. Roukema, "Ultrasonography important as a supplement to mammography". (Dut) *Ned Tijdschr Geneeskd* 137: 2378-2383, 1993.

[6] Perre C.I., de Hooge P., Hustinx P.A. and Muller J.W. "Ultrasonographic study of the palpable breast tumor is very useful." (Dut) *Ned Tijdschr* Geneeskd 137: 2374-2377, 1993.

[7] V.P. Jackson, R.E. Hendrick, S.A. Feig and D.B. Kopans,"Imaging of the radiographically dense breast." *Radiology* 188: 297-301, 1993.

[8] E. Halberg, F. Halberg, G. Cornelissen, M. Garcia-Sainz *et al.* "Toward a chronopsy: part II. A thermopsy revealing asymmetrical circadian variation in surface temperature of human female breasts and related studies." *Chronobiologia* 6: 231-257, 1979.

[9] D.W. Wilson, M.J. Phillips, H.W. Holliday, R.W. Blamey *et al.* "Prolactin and breast skin temperature rhythms in postmenopausal women with primary breast cancer." *Chronobiologia* 10: 21-30, 1983.

[10] M. Gautherie, A.Yahyai, S. Dehlinger, J. De Prins and J.P. Walter, "Computerized chronothermodynamic breast examinations under ambulatory conditions." *Chronobiol Int* 7: 239-243, 1990.

[11] J. Cary, L. Kalisher, N. Sadowsky and B. Mikic, "Thermal evaluation of breast disease using local cooling." *Radiology* 115: 73-77, 1975.

[12] R. Pochaczevsky and P.H. Meyers, "Vacuum contoured, liquid crystal, dynamic breast thermoangiography as an aid to mammography in the detection of breast cancer." *Clin Radiol* 30: 405-411, 1979.

[13] E.E. Sterns and B. Zee,"Thermography as a predictor of prognosis in cancer of the breast." *Cancer* 67: 1678-1680, 1991.

[14] J.F. Head, F. Wang, and R.L. Elliott, "Breast thermography is a noninvasive prognostic procedure that predicts tumor growth rate in breast cancer patients." *Ann.N.Y.Acad.Sci.* 698: 153-158, 1993.

[15] R.L. Elliott, F. Weng, M.W. Hailey and J.F. Head, "The role of thermography in the diagnosis and treatment of breast cancer." Proceedings of this symposium.

[16] M. Anbar, "Hyperthermia of the cancerous breast - analysis of mechanism." *Cancer Lett* 84(1): 26-32, 1994.

[17] M.W. Radomski and S. Moncada, "Regulation of vascular homeostasis by nitric oxide." *Thromb Haemost* 70: 36-41, 1993.

[18] C.J. Lowenstein, J.L. Dinerman and S.H. Snyder, "Nitric oxide: a physiologic messenger." *Ann Intern Med* 120: 227-237, 1994.

[19] J. Klostergaard, "Macrophage tumoricidal mechanisms." *Res. Immunol.* 144: 274-276, 1993.

[20] C.M. Maragos, J.M. Wang, J.A. Hrabie, J.J. Oppenheim and L.K. Keefer, "Nitric oxide/nucleophile complexes inhibit the in vitro proliferation of A375 melanoma cells via nitric oxide release." Cancer Res. 53: 564-568, 1993.

[21] N.R. Bastian, C.Y. Yim, J.B. Hibbs Jr and W.E. Samlowski, "Induction of iron-derived EPR signals in murine cancers by nitric oxide. Evidence for multiple intracellular targets." *J Biol Chem* 269: 5127-5131, 1994.

[22] D.W. Reif and R.D. Simmons, "Nitric oxide mediates iron release from ferritin." *Arch Biochem Biophys* 283: 537-541, 1990.

[23] M. Lee, P. Arosio, A. Cozzi and N.D. Chasteen, "Identification of the EPR-active iron-nitrosyl complexes in mammalian ferritins." *Biochemistry* 33: 3679-3687, 1994.

[24] M. Anbar, J.C. Montoro, K-H. Lee and S. D'Arcy, "Manifestation of neurological abnormalities through frequency analysis of skin temperature regulation." *Thermology* 3: 234-241, 1991.

[25] M. Anbar, "Dynamic Area Telethermometry - A New Field in Clinical Thermology" Part I *Medical Electronics* 146: 62-73, 1994; Part II *Medical* Electronics 147: 73-85, 1994.

[26] F.W. Mohr, V. Falk, H. Krieger, J. Likungu *et al.*, "IMA-graft patency control by thermal coronary angiography during coronary bypass surgery." *Eur J Cardiothorac Surg* 5: 534-541, 1991.

[27] F. Ring, "Quantitative thermal imaging in rheumatology." Proceedings of this symposium.

[28] M. Anbar "Thermological implication of vasodilation mediated by nitric oxide." *Thermologie Osterreich* (in press, 1994)

[29] M. Anbar and R. F. Haverly, "Local "micro" variance in temperature distribution evaluated by digital thermography.", in *Advanced* Techniques *and Clinical Applications in Biomedical Thermology*, K. Mabuchi *et al.* (Eds.) Gordon & Breach, Basel, 1994.

[30] M. Anbar and S. Hejazi, "Infrared fluorescence and light-induced enhanced reflectivity of Different Materials." in: Advanced Techniques and Clinical Applications in Biomedical Thermology, K. Mabuchi *et al.* (Eds.) Gordon & Breach, Basel, 1994.

THE ROLE OF THERMOGRAPHY IN THE DIAGNOSIS AND TREATMENT OF BREAST CANCER

Robert L. Elliott, Fen Wang, Michael W. Hailey and Jonathan F. Head
The Elliott Mastology Center, 1770 Physicians Park Drive, Baton Rouge, LA 70816

ABSTRACT

Breast thermography is a noninvasive procedure that can detect abnormal heat patterns of the breast. The importance of these abnormalities as a high risk marker, in diagnosis of breast cancer and especially as a prognostic indicator in breast cancer has not been appreciated by the oncology community. This has led to breast thermography not being included as a diagnostic procedure in routine screening or as a prognostic procedure to be integrated with other prognostic indicators in determination of therapy. The occurrence of abnormal thermographic patterns in three categories of patients was found to be 28% (28/100 patients) for normal patients without breast cancer, 65% (65/100 patients) for living breast cancer patients and 88% (111/126 patients) for deceased breast cancer patients. Twenty of the cancer patients had thermography done at least twice with one of their thermograms being done a minimum of one year before biopsy of the cancerous lesion. Fifty percent (10/20) of the patients in this subgroup had abnormal thermograms at the time of biopsy and therefore this subgroup is representative of the whole breast cancer group. Seven of the 10 patients with positive thermograms at biopsy had positive thermograms at least one year prior to biopsy with a median of 87 months (range 18 to 158 months), and all ten of the breast cancer patients with normal thermograms at biopsy had normal thermograms for a median of 95 months (range 24 to 123 months). These results demonstrate that an otherwise normal patient with an abnormal thermogram should be considered at high risk for breast cancer. These results further show that a breast cancer patient with an abnormal thermogram has a poorer prognosis and therefore should be treated with more aggressive adjuvant therapy.

Key Words: Thermography, Diagnosis, Prognosis, Breast Cancer

INTRODUCTION

The application of thermography to the diagnosis of breast cancer was initiated in the 1970s in both Europe and the United States. The Breast Cancer Detection and Demonstration Projects (BCDDP) sponsored by the National Cancer Institute (USA) from 1973 to 1981 were designed to test the role of both thermography and mammography in the diagnosis of breast cancer but the part of the study involving thermography was discontinued very early in the study. The premature closing of the thermography part of the BCDDP study was due to technical difficulties, lack of training, lack of experience, lack of standardization of equipment, and lack of interest in this new technology by Radiologists. The closure resulted in there being no clear demonstration of the possible importance of thermography in the diagnosis of breast cancer. Another result of discontinuation of the part of the study designed to test the diagnostic ability of thermography in breast cancer was that no data was collected to prove the diagnostic superiority of mammography over thermography, to evaluate thermography as an indicator of risk of developing breast cancer, or to evaluate it as a prognostic indicator in patients with abnormal mammograms, who later were surgically biopsied and diagnosed with breast cancer.

After the BCDDP closed their study of thermography several studies have supported the role of thermography as a high risk marker for breast cancer [1, 2], in the diagnosis of breast cancer [1, 2, 3] and as a prognostic indicator for breast cancer patients [3, 4]. The results reported in this study further support the use of thermography in risk assessment and as a prognostic indicator, but additional studies are needed to see if thermography can be used in determining which node negative breast cancer patients should receive adjuvant chemotherapy.

METHODS

The normal and breast cancer patients for this study were selected from patients who had undergone breast thermography as part of their breast examination at the Elliott Mastology Center beginning in 1973. Their breast exams also included mammography and clinical examination. The group for this study included three categories of patients: 126 patients that died of breast cancer during this period and had breast thermography within the one year period leading up to diagnosis of their breast cancer, 100 randomly selected living breast cancer patients who also had thermography within the one year period previous to their diagnosis of breast cancer, and 100 patients who have not been diagnosed as having breast cancer and had breast thermography. If during thermographic examination asymmetric heat patterns (diffuse heat, focal hot spots, areolar and/or periareolar heat, vessel discrepancy or thermographic edge signs) were noted then the patient displaying this abnormal breast pattern was considered to be at high risk of getting breast cancer or to have a poor prognosis, if already diagnosed with breast cancer. Clinical/pathological staging (tumor size, nodal status, presence of metastasis), age, and location of the cancer were also done for all breast cancer patients and the results were compared to thermographic results.

RESULTS

When the thermographic results of the patients were divided into three groups of normal, cancer and deceased cancer patients it is clear that there is a greater percentage of cancer patients with abnormal thermograms than patients at normal or high risk of developing breast cancer (Table 1).

TABLE 1. Thermographic Results for Normal, Cancer, and Deceased Patients

Thermographic Results	Patients		
	Normal	Cancer	Deceased
Normal	72 72%	35 35%	15 12%
Abnormal	28 28%	65 65%	111 88%

$p<.0001$, chi-square analysis for independence

There was a 28% incidence of abnormal thermograms in normal patients, and a significantly greater incidence at diagnosis of 65% for living breast cancer patients and 88% for deceased breast cancer patients. The 88% incidence of abnormal thermograms in the deceased breast cancer patients at diagnosis was also significantly higher than the 65% incidence of breast cancer patients in general. The data in Table 1 shows that the increasing incidence of abnormal thermograms is significantly related to the likelihood of progression or to progression of the disease, and thus thermographic results also have prognostic significance.

The prognostic significance of the components of the clinical/pathological staging system have previously been demonstrated in breast cancer patients. In this study we found that nodal status and presence of metastatic disease were not related to thermographic results. However, clinical tumor size, but not pathological tumor size, was significantly related to thermographic findings, which resulted in patients with larger tumors being more likely to have an abnormal thermogram (Table 2).

TABLE 2. Chi-Square Analysis for Independence of Clinical Tumor Size and Thermographic Results

Thermographic Results	Clinical Size Classification		
	T1 (<2 cm)	T2 (2-5 cm)	T3 (>5 cm)
Normal	9	14	0
Abnormal	10	31	10
% Abnormal	53	69	100

$p<.05$, chi-square analysis for independence

Even though patients with larger tumors were more likely to have an abnormal thermograms it is important to note that the group of patients with the smallest tumors (T1) also had over 50% abnormal thermograms. The age of the patients (less than 50 compared to greater than or equal to 50) and location of the tumor (left compared to right breast) were also found to be independent of and therefore unrelated to thermographic results.

Table 3 presents the results on twenty cancer patients from this study that had serial thermography done and had at least one thermogram done a minimum of one year before being diagnosed with breast cancer.

TABLE 3. Thermographic Results of Patients Who Had a Thermogram at Least One Year Before Diagnosis and at Diagnosis of Breast Cancer

Thermographic Results at Least One Year Prior to Diagnosis	Thermographic Results at Diagnosis	
	Normal	Abnormal
Normal	10	3
Abnormal	0	7

$p<.005$, chi-square analysis for independence

These twenty patients had thermographic results at diagnosis that are representative of the larger group that they were selected from in that 50% (10 of 20 patients) had abnormal thermograms, which is similar to the 65% (65 of 100 patients) with abnormal thermograms from Table 1. All ten of the patients that had normal thermograms at diagnosis had normal thermograms at least one year before diagnosis and a large proportion (70%) of the patients that had abnormal thermograms at diagnosis of breast cancer had abnormal thermograms at least one year prior to diagnosis. A small proportion (30%) of patients with abnormal thermograms at diagnosis previously had normal thermograms. The average times between earliest positive or negative thermogram and diagnosis is presented in Table 4.

TABLE 4. Length of Time of Follow-up

Thermographic Results		Number of Patients	Follow-up Time in Months		
>1 Year Before	At Diagnosis		Mean$\pm$SD	Median	Range
Abnormal	Abnormal	7	95$\pm$46	87	18-158
Normal	Normal	10	90$\pm$30	95	24-123
Normal	Abnormal	3	34$\pm$19	24	23-56

The 7 patients with abnormal thermograms at diagnosis, who had abnormal thermograms at least a year earlier, had abnormal thermograms for an average of almost 8 years. The 10 patients with normal thermograms at diagnosis had normal thermograms for an average of 7.5 years. The few patients that change from normal thermograms to abnormal at diagnosis had normal thermograms at least 23 months before diagnosis.

DISCUSSION

To date thermography of the breast has not been adequately studied for conclusions to be drawn about its role in the diagnosis of breast cancer. In the BCDDP thermography was originally included in the study but was quickly discontinued without collection of the data necessary to determine the diagnostic value of breast thermography. The high false positive rate (found to be 28% in the present study) of thermography compared to mammography in normal patients has always been considered a major drawback of thermography. The combination of this high false positive rate with the inability of thermography to localize a lesion or tumor (thermographic abnormalities do not define an area that can be surgically biopsied for cancer) has been sufficient reason to prevent breast thermography from becoming a routine procedure used in the diagnosis of breast cancer.

This high false positive rate does suggest that breast thermography might be useful in defining a group of patients at high risk for breast cancer. It is obvious that any group of patients who are undergoing mammography and thermography are at a higher than normal risk of developing breast cancer and therefore their risk exceeds the 10% risk of women in the general population. Gautherie and Gros [1] showed that 38% (298/784) of patients with abnormal thermograms were diagnosed with breast cancer in the 4 year period following the abnormal thermograms, and Stark [2] found that 23% of patients with abnormal thermograms developed breast cancer within 10 years. In the present study the significantly ($p<.0001$, chi-square analysis for independence) higher percentage (65%) of patients with abnormal thermograms at diagnosis compared to the 28% rate of abnormal thermograms in the normal and high risk patients suggests that an abnormal thermogram is a high risk marker in breast cancer. This suggestion is reinforced by the data in Table 4 where it can be seen that 35% (7/20) of the cancer patients had abnormal thermograms 18 to 158 months prior to their diagnosis of breast cancer. These studies all provide strong evidence that breast thermography, an inexpensive and completely noninvasive procedure, has an important role in defining a group of women at high risk for breast cancer. These patients at increased risk of developing breast cancer should have mammography, thermography and clinical examination more frequently in an attempt to diagnose their breast cancer at an earlier and more curable stage.

Since the mid 1980s breast cancer researchers have been searching for clinical, pathological and biochemical characteristics of breast cancer that can be integrated to provide a rational basis of selecting node negative (absence of spread of the breast cancer to the axillary lymph nodes under the arm) breast cancer patients for adjuvant chemotherapy. It is known that breast cancer in approximately 90% of node negative patients with tumors less than 2 cm in diameter will not recur and cause death, but will recur in approximately 10% of the patients and after recurrence will be less responsive to chemotherapy than it would have been in the adjuvant setting. Thermography appears to provide prognostic information that could be used in combination with other clinical, pathological and biochemical parameters in the selection of node negative breast cancer patients for adjuvant chemotherapy. Isard *et al* [4] in a study of 70 breast cancer patients showed that 30% of patients with abnormal thermograms survived 5 years compared to 80% of patients with normal thermograms. The present study showed that 65% of the breast cancer patients had abnormal thermograms, but a significantly ($p<.0001$, chi-square analysis for independence) greater proportion (88%) of the breast cancer patients who had died of breast cancer had abnormal thermograms. This significantly greater proportion of deceased breast cancer patients with abnormal thermograms is further evidence to support thermography as a prognostic procedure for breast cancer patients.

It is important to determine if thermographic results have prognostic value independent of other previously identified prognostic indicators. We have previously reported that when thermography was done at the same time as diagnostic mammography (prior to diagnostic needle or surgical biopsy for breast cancer) and compared to the size, nodal status and presence of metastatic disease of the TNM classification system, then thermographic results were only related to clinical tumor size (see Table 2). It is important to note, that even though the percentage of patients with abnormal thermograms increased with increasing tumor size, that over 50% (10 of 19) of the patients with small tumors (less than 2 cm in diameter) had abnormal thermograms. This suggests that increased risk of recurrence could be related to thermographic results even in the group of patients with tumors less than 2 cm in diameter. When looking at all stages of breast cancer thermographic results were independent of nodal status, but we do not have enough Stage I (a tumor less than 2 cm in diameter, negative

lymph nodes and free of metastatic disease) breast cancer patients to analyze their thermographic results in terms of adjuvant chemotherapy. Head *et al* [3] also showed that thermographic results were unrelated to age, tumor location (right or left breast), and estrogen and progesterone receptor status. Many more patients will have to be analyzed to confirm that thermography is an independent and useful prognostic indicator, and we feel that this would be a worthwhile pursuit considering the small cost and noninvasive nature of thermography.

The growth rate of breast cancers, determined by measuring the change in diameter of breast tumors over time and calculating tumor volume doubling times, has been shown to be one of the best predictors of disease free and overall survival and therefore is a good prognostic indicator in breast cancer patients. However the clinician is rarely able to follow a growing tumor in individual patients over a long enough period of time to determine the volume doubling time of their breast cancer. It will be necessary to find a more practical method of approximating growth rate or other more easily determined prognostic indicators that are highly correlated to and dependent on growth rate in breast tumors. Tumor growth rate [5], tumor ferritin concentration [3], proliferation index by flow cytometry [3] and semiquantitation of the proliferation-associated antigen Ki-67 in frozen sections by immunocytochemistry [3] have all been shown to be related to thermographic results. The correlation of growth rate and these proliferation-related parameters with thermographic results suggests that a breast cancer patient with an abnormal thermogram has a higher probability of having a fast growing tumor with increased blood flow to the tumor and the tissue immediately surrounding that tumor. This increased blood flow is necessary to bring the nutrients required to maintain the growth rate of fast growing tumors and is probably responsible for the thermographic abnormalities observed in the thermograms of breast cancer patients. The most remarkable aspect of thermography is that these abnormalities often precede mammographic abnormalities associated with breast cancer by years and sometimes even decades [1, 2]. We therefore believe that the higher metabolic rate of faster growing tumors and the associated increase in local vascularization causes most of the abnormalities seen in the thermography of breast cancer patients. Since faster growing tumors are known to have poorer prognosis the association of these fast growing tumors with abnormal thermographic results accounts for thermography having prognostic value for breast cancer patients.

CONCLUSIONS

The role of breast thermography for diagnosis of breast cancer, in risk assessment for breast cancer and as a prognostic indicator in breast cancer has not been fully determined. The use of thermography diagnostically is limited by its inability to localize the tumor and therefore thermography can only be used to complement mammography in the diagnosis of breast cancer. Thermography does have an important role in the determination of breast cancer risk for women and the evidence presented here demonstrates that women with abnormal thermograms are at increased risk, approaching 30%, of developing breast cancer. These high risk patients should be followed closely with thermography, mammography and clinical examination in order to detect their cancers early, when there is a higher probability of cure. Thermography also has prognostic value for the breast cancer patient and thermographic results in Stage I breast cancer patients should be integrated with the results of other prognostic indicators when deciding whether to give adjuvant chemotherapy.

REFERENCES

1. **Gautherie M, and Gros CM:** Breast thermography and cancer risk prediction. *Cancer* 45: 51-56, 1980.

2. **Stark AM:** The value of risk factors in screening for breast cancer. *Eur. J. Cancer* 11: 147-150, 1985.

3. **Head JF, Wang F, and Elliott, RL:** Breast thermography is a noninvasive prognostic procedure that predicts tumor growth rate in breast cancer patients. *Ann. N. Y. Acad. Sci.* 698: 153-158, 1993.

4. **Isard HJ, Sweitzer CJ, and Edelstein GR:** Breast thermography: A prognostic indicator for breast cancer survival. *Cancer* 62: 484-488, 1988.

5. **Gautherie M:** Thermography of breast cancer: Measurement and analysis of the *in vivo* temperature and blood flow. *Ann. N. Y. Acad. Sci.* 335: 383-413, 1982.

PRE- AND POSTOPERATIVE THERMOGRAPHIC IMAGING ON THE LUMBAR DISC HERNIATIONS

Young-Soo Kim, M.D., Yong-Eun Cho, M.D.

Spine Center, Department of Neurosurgery, Yongdong Severance Hospital,
Yonsei University College of Medicine
Seoul, Korea

Thermography reveals the skin temperature changes in various conditions of the body. The skin temperature changes according to the sub-cutaneous blood flow under the control of autonomic nervous system. In radiculopathy by lumbar disc herniation, the discogenic pain provokes the change in sympathetic function of the nerve root via sinuvertebral nerve stimulation and changes skin temperature along the nerve root. Digital infrared thermographic imaging system has been used for diagnosis of radiculo-pathy without hazard of radiation or pain and it can measure the temperature changes due to discogenic pain objectively.

Authors analyzed pre- and postoperative thermographic imaging in 1,458 cases of lumbar disc herniations. Digital infrared thermographic imagings revealed high sensitivity to clinical symptoms as 89.5% and other radiological studies. Anatomical level of disc herniation in thermographic examination was equal to other radiological examination such as myelography, CT scan, MRI in 79.1%, 78.8%, 76.6% respectively. Thermographic pattern of lumbar disc herniation were classified into three types; radiculopathy pattern, spot pattern, nonspecific pattern and thermatome of each nerve root was analyzed.

After surgery, changes of thermal distribution and thermal difference compared to preoperative imagings were analyzed. Thermographic results after operation were closely correlated with postoperative clinical results as 82.4%.

Digital infrared thermographic imaging is considered as a very useful for diagnosis of lumbar disc herniation and for follow up of clinical results. It shows high sensitivity to clinical symptom and equality to anatomical level in diagnosis of disc herniation and high validity in evaluation of postoperative course.

KEY WORDS: Thermography. Lumbar disc herniation. Sensitivity . Validity

Introduction

Since Lawson reported clinical application of thermography in 1956[13], infrared thermographic imaging technique has been used for diagnosis of breast diseases, autonomic nervous system disorders, radiculopathies, peripheral nerve injury, inflammatory disorders because it can reveal the pain objectively without pain and radiation hazard during examination.[1)3)15)17)22)] There are many papers about infrared thermographic findings in disc herniations since Pochaczvsky reported the usefulness of infrared thermography in radiculopathy.[2)12)15)18)20)21)] Early thermographic techniques were contact types using liquid crystal of cholesterol esters.[3)9)20)21)] But it was inaccurate because of low sensitivity to thermal changes and technical difficulties. With development of computer engineering, thermographic imaging techniques were remarkably developed.[16)] Now it needs not contact to body surface and can measure body temperature more accurately with outstanding color presentation. So it is used in medical fields such as neurosurgery,[2)11)] orthopedics, pain clinic,[14)] otolaryngology, urology[10)] etc.

11,136 cases of infrared thermographic examinations in various spinal diseases are performed in our department from April 1990 to August 1994. Among them preoperative and postoperative thermographic findings of 1,458 patients taken operations due to lumbar disc herniation were analyzed.

Materials & Methods

Preoperative and postoperative digital infrared thermographic findings of 1,458 patients who had operation due to lumbar disc herniation in Spine center, Department of Neurosurgery, Yonsei University College of Medicine, Seoul, Korea from April 1990 to August 1994. All patients had typical clinical symptoms such as low back pain, radiating leg pain and abnormal lumbar disc protrusion in CT scan or MRI. Preoperative and postoperative Digital Infrared Thermographic Imagings were taken in all patients. They were taken in closed room with constant temperature, humidity, air flow by Digital Infrared Thermographic Imaging (DITI, DOREX Inc. U.S.A.). We measured the temperatures of lumbosacral area, whole leg, dorsum of feet and soles.

Preoperative thermographic imagings were classified according to thermatomal pattern and thermatome of each lumbar nerve root was analyzed in single, unilateral disc herniation.

The postoperative thermographic findings were compared with preoperative findings. The changes of thermal difference after surgery and correlation with clinical rersults were evaluated.

Results

1. Age and sex distribution

Among 1,458 patients, sex ratio was 2.1:1 with male predominance. The patient's age ranged from 14 to 70 years was most frequent in third decade and 5th decade, 4th decade, 6th decade, 2nd decade in order(Table 1).

Table 1. Age and sex distribution

Age	Male	Female
10 - 20	85	53
21 - 30	312	89
31 - 40	202	114
41 - 50	241	155
51 - 60	114	53
61 - 70	35	5
Total	989	469

2. Distribution of lumbar disc herniations

Lumbar CT scan or MRI examinations were performed in all cases. Disc herniation was most frequent in L4/5(839 cases, 57.6%) and L5/S1 next common(276 cases, 18.9%) and multiple disc herniations were 323 cases.(Table 2).

Table 2. Levels of disc herniation levels(N=1,458)

Levels	Cases	%
L2/3	3	0.2
L3/4	17	1.2
L4/5	839	7.6
L5/S1	276	18.9
Multiple	323	22.1
L2/3 + L3/4	2	0.1
L3/4 + L4/5	90	6.1
L4/5 + L5/S1	222	15.3
L3/4 + L4/5 + L5/S1	9	0.6

3. Operative methods

During from April 1990 to August 1994, total 1,458 cases of lumbar spinal surgery for lumbar disc herniation were performed. Among them, herniations, laminectomy and discectomy was done in 902 cases and the rest (556 cases) was performed chymopapain chemonucleolysis.

4. Patterns of thermographic findings

Thermographic findings were analyzed by the patterns of temperature change in 1,458 disc patients preoperatively. Thermal asymmetry between both legs and thermal differences(ΔT) were analyzed between symptomatic side and non symptomatic side.

Abnormal thermographic findings were defined that thermal difference(ΔT) of both legs was over 0.5 $^{\circ}$C or even though ΔT was less than 0.5 $^{\circ}$C, the thermal change was noted at the same area equal to painful site and revealed along nerve distribution.

The thermographic patterns were classified into radiculopathy type, spot type, nonspecific patterns(Figure 1). The radiculopathy pattern showed hypo- or hyperthermia along the nerve root. Spot pattern showed localized thermal change at pain area and nonspecific pattern showed no specific thermal difference in both legs. In analysis of preoperative thermographic findings, radiculopathy patterns were most frequent as 1,226 cases(84.1%) and nonspecific pattern(153 cases, 10.5%), spot pattern(79 cases, 5.4%) in order. Among 1,226 cases of radiculopathy pattern, ipsilateral hypothermia equal to symptomatic side was 82.8%(1,015 cases). Ipsialteral hyperthermia or contralateral hypothermia revealed in 7.5%(109 cases). The mixed patterns of hypothermia and hyperthermia were 142 cases(Table 3).

Table 3. Thermographic patterns(Thermatome) in disc herniations(N=1,458)

Patterns of thermatome	Cases	%
Radiculopathy pattern	1226	84.1
Ipsilateral hypothermia	1015(82.8%)	
Ipsilateral hyperthermia (=contralateral hypothermia)	109(7.5%)	
Mixed	142(9.7%)	
Spot pattern	79	5.4
Nonspecific pattern	153	10.5

5. L5 thermatome

Thermographic findings of single unilateral L4/5 disc herniation(839 cases) were analyzed. Among them radiculopathy type is most common(81.9%) and nonspecific type(12.1%), spot type(6.0%) in order. The areas of thermal change in radiculopathy type(687 cases) were investigated and thermatome of L5 root was analyzed(Figure 2). L5 thermatome was noted at buttock, thigh with extension to calf, dorsum of foot along the medial aspect of shin. At the sole medial aspect was much colder than lateral aspect(Figure 3).

6. S1 thermatome

S1 thermatome was investigated by analysis of 276 cases revealed unilateral single level disc herniation at L5/S1 level. Among them radiculopathy type was 223 cases(81.3%) and spot type was 24 cases(8.5%) and nonspecific type was 29 cases(10.2%). The area of thermal change in radiculopathy type(223 cases) were investigated and the thermatome of S1 root was analyzed(Figure 2). S1 thermatome was revealed as hypothermia on leg extending from the lateral aspect of buttock to posterolateral thigh, lateral aspect of shin, heel along the nerve root. At the sole lateral aspect was colder than medial aspect of sole(Figure 4).

7. L3 & L4 thermatome

Thermography of L3/4 disc herniation(17 cases) was analyzed for L4 thermatome. The L4 thermatome showed hypothermia on anterior and lateral aspect of thigh mainly. L3 thermatome by L3 root compression was studied with 3 cases of L2/3 disc herniation and it revealed hypothermia on lateral aspect of thigh mainly(Figure 5).

8. Clinical value of Digital Infrared Thermographic Imaging

For estimate of clinical value of DITI, Thermographic findings of DITI were compared with clinical symptoms such as low back pain, radiating leg pain and radiological studies as myelography, CT scan, MRI. The DITI was highly sensitive as 89.5% to clinical symptoms and in radiological studies it was well correlated with myelography, CT scan, MRI such as 86.9%, 85.2%, 87.0%

respectively(Table 4). The accuracys of DITI equal to anatomical level of lesion in myelography, CT scan, MRI scan was high such as 79.1%, 78.8%, 76.6% respectively(Table 5).

Table 4. Sensitivity of DITI

	Sensitivity
Clinical symptoms(N=1458)	1305/1458(89.5%)
Myelography(N=110)	97/110(86.9%)
CT scan(N=1447)	1233/1447(85.2%)
MRI scan(N=604)	525/604(87.0%)

Table 5. Equality to anatomical level

	Myelography (N=110)	CT scan (N=1447)	MRI (N=604)
DITI	87/110 (79.1%)	1140/1447 (78.8%)	463/604 (76.6%)

9. Postoperative course

In 1458 patient undergone surgery, overall postoperative clinical results were as follows; excellent 50.1%, good 40.6%, fair 5.5%, poor 3.9% (Table 6). Postoperative DITI examination was done in 1226 cases among 1458 patients undergone surgery. Thermal difference between pre and postoperative thermographic imaging was analyzed and according to change of thermal difference, thermographic outcome was classified(Table 7). On thermographic outcome, excellent was 345 cases(28.2%) and good was 579 cases(47.3%). In 151 cases, poor group, hypothermia at the lesion side was aggravated compared to preoperative state and thermal difference was increased(Table 10).

Table 6. Postoperative clinical results(N=1458)

Results	Cases	%
Excellent	730	50.1
Good	592	40.6
Fair	80	5.5
Poor	56	3.9

Table 7. Postoperative thermographic outcome

Excellent	Much improved ΔT($\Delta T < 0.5$ °C, nearly symmetrical)
Good	Improved ΔT($\Delta T > 0.5$ °C, decreased ΔT)
Fair	No interval change
Poor	More hypothermia compared to preoperative studies

Table 8. Postoperative therrmographic results (N=1226)

Results	Cases	%
Excellent	345	28.2
Good	579	47.3
Fair	151	12.3
Poor	151	12.3

10. Correlation between clinical and thermographic outcome

Clinical and thermographic outcomes were analyzed in 1226 patients taken preoperative and postoperative DITI examinations. Among patients with good to excellent clinical outcome, 874 cases

showed good to excellent thermographic outcome. In fair to poor clinical group, 136 cases revealed fair to poor thermographic result. Overall validity of DITI examination was 82.4%(Table 9).

Table 9. Comparison of results between clinical and thermographic results(N=1226)

DITI Results	Clinical Results				
	Excellent	Good	Fair	Poor	Total
Excellent	184	146	7	8	345
Good	304	240	25	10	579
Fair	56	31	34	30	151
Poor	44	34	41	31	151

Discussion

Lumbar disc herniation causes severe low back pain and radiating leg pain. But the symptoms are subjective according to patient and the complaints of symptoms are variable such as numb, tingling, lancinating, etc. So it is hard to approve the symptoms objectively and exact mechanisms of each symptoms are still unknown.

Thermography is the examination tool that can detect the abnormal condition of body with invisible infrared ray radiating from body. Temperature change of body has been used in medical field since Hippocrates and the scientific base of thermography was made by Willam Herschel who classified universal ray and named the invisible ray with long wave length, high energy as infrared. In 1948 Leo Massopurt started clinical application of thermography and Lawson reported for the first time thermographic change in breast cancer.[14] In neuromuscular diseases Pochazevsky and Wexler reported that thermography was useful for diagnosis of radiculopathy including disc herniation by contact thermography in 1983[18]. Mills studied the temperature of each part of body in lumbar stenosis patients with objective comparative method[15].

Contact liquid crystal thermography had limited value due to unacceptable color change according to temperature change and unreliable objectivity. Also it had a limit in examination of curved area and it could not examine wide area of body.

As the development of computer engineering, limits of contact liquid crystal thermography were overcome. Digital infrared thermographic imaging technique can detect the infrared from body by sensor and can measure body surface temperature exactly. It can take the image without contact to body and can be examined in more comfortable condition without radiation hazards or pain caused by other radiological or physiological examinations.

Thermographical change in lumbar disc herniation is under the influence of recurrent meningeal nerve(sinuvertebral nerve)[7][8]. The sinuvertebral nerve branches from ventral ramus of spinal nerve and the sinuvertebral nerve reenters into vertebral canal via intervertebral foramen . It has connection with sympathetic nervous system via gray ramus communicants and innervates posterior longitudinal ligament, dura, outer layer of annulus fibrosus and periosteum[8]. It can overlap one or two segment in upper and lower level and can cross the midline with contralateral innervation[4][7]. When lumbar disc protrusion occurs, it activates sinuvertebral nerve and stimulates the sympathetic nervous system. It causes a peripheral vasoconstriction over the area of sympathetic innervation and hypothermia over the skin is resulted. At the same time cutaneous branch of dorsal ramus of spinal nerve which innervates over posterior lumbosacral area causes localized vasodilatation by antidromic stimulation and localized hyperthermia is noted in anatomical level at the midline of posterior back[5][11][18][19][21] (Figure 6).

In this study, 1458 cases of thermographic images were analyzed in lumbar disc herniation and the types of thermographic pattern were classified as radicular pattern, spot pattern and nonspecific pattern. Radicular thermographic pattern which showed localized hyperthermia at anatomical level and hypothermia along the leg was appeared in 1226 patients(84.1%). Among radicular pattern, typical ipsilateral hypothermia was noted in 1015 cases(82.8%) and contralateral hypothermia(ipsilateral hyperthermia) was identified in 109 cases(7.5%). About contralateral hypothermia Hubbard[7] and Kim[11] reported the incidence such as 10.0%, 4.8% respectively.

Mechanisms of contralateral hypothermia were uncertain but those were suspected such as 1)contralateral innervation of sinuvertebral nerve, 2)peripheral vasodilatation due to complete denervation of ipsilateral sympathetic function, 3) axonal reflex caused by hyper acute severe disc herniation. Mixed pattern with hypothermia and hyperthermia was noted in 9.7% among radiculopathy pattern.

Nonspecific pattern which showed no definite thermal difference between both legs was 153 cases (10.5%) and localized thermal change was noted in 79 cases(5.4%).

Pierre LeRoy defined a thermatome as cutaneous vascular association area.[6] and Pochaczevsky made schematic drawings of thermatome in cervical and lumbar radiculopathies.[18] In this study we analyzed the thermatomes of each lumbar nerve root were studied in cases with typical radicular pattern.

S1 thermatome was characterized by localized hyperthermia on lumbosacral region and ipsilateral hypothermia of posterolateral thigh, calf radiating to heel, lateral aspect of shin, lateral aspect of sole. L5 thermatome was characterized by ipsilateral hyperthermia on lumbar area and hypothermia of the ipsilateral mid - and lateral gluteal region, anterolateral thigh, medial aspect of shin radiating to dorsum of foot, medial aspect of sole. L4 thermatome revealed as hypothermia on anterolateral aspect of upper thigh. and L3 thermatom showed hypothermia on lateral aspect of thigh.

The sensitivity of DITI to clinical symptoms was 89.5% in this study and it was similar with reports of Abram, Pulst, Uematsu[21], Hubbard[12], Wexler, Kim[11], Cho[2] showed sensitivity such as 76-100%. Analysis of sesitivity of DITI comparing with radiological studies showed high sensitivities such as 85.2% to myelography, 85.2% to CT scan, 87.0% to MRI scan. EMG cases were rare so it was impossible to study sensitivity of DITI to EMG, other physiologic study.

The anatomical location of lesion in DITI examination was investigated in the cases which had radiologic evidences in myelography or CT scan, MRI scan and confirmed antomical level by surgery. The equality of anatomical level in DITI eaxamination was relatively high such as 79.1% with myelography, 78.8% with CT scan, 76.6% with MRI.

In current study postoperative clinical result was as followings; excellent 50.1%, good 40.6%, fair 5.5%, poor 3.8%. Overall success rate was 90.7%. Postoperative clinical results in chymopapain chemonucleolysis group and laminectomy group were compared. In chemonucleolysis group success rate was 87.0%(excellent 45.5%, good 41.5%) and success rate of laminectomy group was 93.2 %.

Preoperative ipsilateral hypothermia was improved after chemonuclelysis or laminectomy and the thermal difference was decreased. The postoperative thermographic result was classified into four groups according to author's criterior for analysis the correlation between clinical result and thermographic result. In analysis of postoperative thermographic result, excellent was 28.2% and good was 47.3%. Fair group was in 12.3% and poor group was 12.2% among all patients. So overall improvement rate after surgery was 75.8%. In chemonucleolysis group, the thermographic results were as followings; excellent 30.2%, good 48.7%, fair 11.1%, poor 10.0%. Overall improvement rate in chemonucleolysis group was 78.9%(Figure 7). In laminectomy group, excellent result was 27.1% and good result was 46.5%. So improvement rate was 73.6%(Figure 8).

With comparision of clinical results and thermographical results in 1226 operated patients, 1010 patients showed equal results in postoperative clinical and thermographical course and the validity of DITI was 82.4%. In 17.6 % of patients there was discrepancy between clinical results and thermographical results. Among them 165 cases(13.4%) showed good to excellent clinical results but their thermographical results were fair to poor. This difference between clinical and thermological results appeared in patients who had massive ruptured lumbar disc or in cases had disc with lumbar stenosis or had previous multiple lumbar operations. The discrepancy was more frequent in laminectomy group than chemonucleolysis group and it was suspected by nerve root trction or irritation during operation. In cases of discrepancy thermal changes were appeared as postoperative numbness, paresthsia, coldness etc.

In conclusion, the analysis of preoperative and postoperative DITI examination in 1226 operated patients revealed that DITI was a reliable, physiologic examination for demonstration of pain objectively and it showed high sensitivity and accuracy with clinical symptoms and radiologic studies. So it was considered very useful in diagnosis of lumbar disc herniations. Postoperative thermographic examination showed high validity with postoperative clinical results as 82.4% and DITI was effective for follow up of postoperative clinical results.

References

1. Belsford KL, Uematsu S: Thermographic presentation of cutaneous sensory and vasomotor activity in the injured peripheral nerve. J Neurosurg 62:711-715,1985
2. Cho J, Moon CT, Na JH et al:Postoperative evaluation of lumbar disc herniation using digital infrared thermographic imaging. J Kor Neuroserg 20(7):528-534,1991
3. Cho WS, Jun WK, Kim JS et al: Clinical study of X-ray mamography and thermography in breast disease. J Kor Radio 25(6):930-936,1989
4. Gandhavadi B, Rosen JS, Addison RG: Autonomic pain. Featurees and methods of assessment. Postgraduate Medicine 71(1):1982
5. Hobbins WB: Basic concept of thermology and its application in the study of the sympathetic nervous system. 1986
6. Hobbins WB: Thermography and pain update(presented at American Academy of Thermology), 1983
7. Hubbard JE: Pain evaluation by electrical infrared thermography: Correlation with symptomes, EMG, myelogram and CT scan.
8. Jinkins JR, Whittemore AR, Bradley WG: The anatomical basis of vertebrogenic pain and the autonomic syndrome associated with lumbar disc extrusion. American Journal of Neuroradiology 10:219-231, 1989
9. Kim JS, Chung YS, Lee MK, et al: Liquid crystal contact thermography in lumbar radiculopathy. J Kor Radiology 22(4):517-521,1987
10. Kim YC, Choi HY, Choi HK: The penile and scrotal temperature by thermography in normal adult Korean. J Kor Med Asso 34(3):321-328,1991
11. Kim YS, Cho YE, Oh SH: Digital infrard thermographic imaging in lumbar disc herniation. Journal of Korean Neurosurgical Society 19:1303-1313,1990
12. Lawson C: The validationof thermology. The American Chiropractor Feb:1989
13. Lawson R: Implications of urface temperatures in the diagnosis of breast cancer. Canad MAJ 75:309-310,1956
14. Lee KC, Lee JK, Woo NS et al: The clinical experience with computer aided thermography during treatment of Bell's pal[illegible]. J Kor Pain Society 4(1):47-50,1991
15. Mills GH, Davie C[illegible], Getty CJM et al: The evaluation of liquid crystal thermography in the investigation of nerve root compression due to lumbosacral lateral stenosis. Spine 11(5):427-432,1986
16. Pireno A, Ricciardi D: The accuracy and objectivity of computer-aided thermographic examinations. The American Chiropractor June,1986
17. Pochaczevsky R, Pillari G, Feldman F: Liquid crystal contact thermography of deep venous thrombosis. AJR 138:717-723,1982
18. Pochaczevsky R, Wexler CE, Meyers PH et al:Liquid crystal thermography of the spine and extremities. Its value in the diagnosis of spinal root syndromes. J Neurosurg 56:386-395,1982
19. Uematsu S: Thermography, in Youmans: Neurological Surgery. 3rd ed., Saunders, 1990, Vol 1, pp 500-508
20. Uematsu S, Edwin DH, Jankel WR et al: Quantification of thermal asymmetry. Part 1: Normal values and reproducibility. J Neurosurg 69:552-555,1988
21. Uematsu S, Jankel WR, Edwin DH et al: Quantification of thermal asymmetry. Part 2:Application in low-back pain and sciatica. J Neurosurg 69:556-561,1988
22. Wood EH: Thermography in the diagnosis of cerebrovascular disease. Thermology 2(1):34 -44,1986

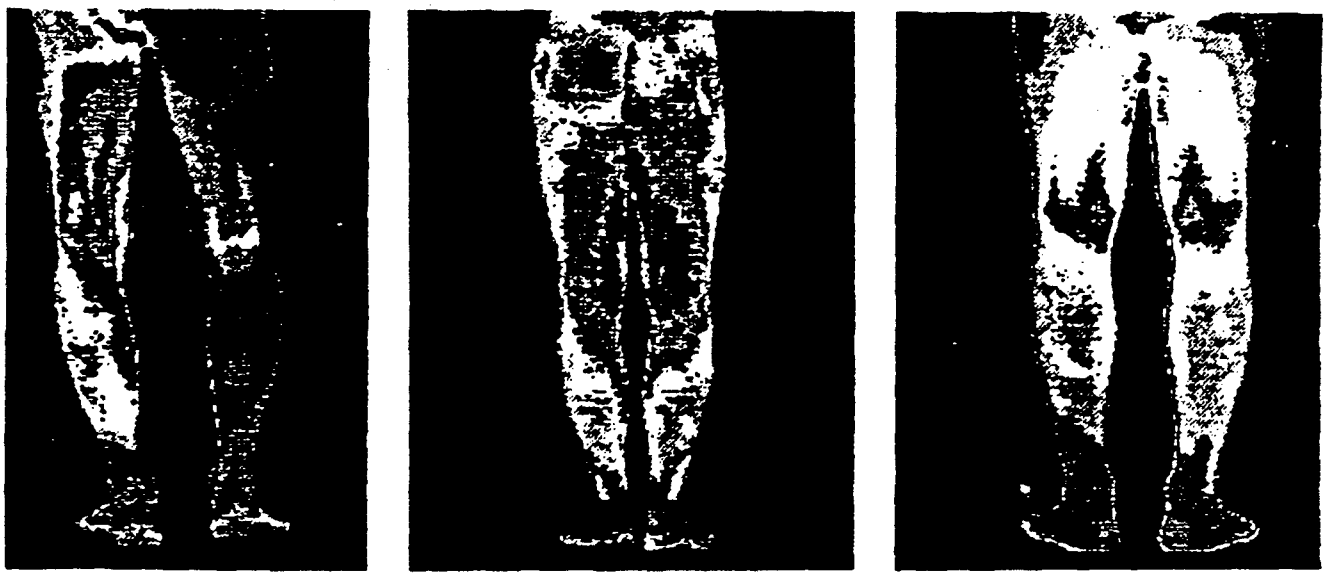

Figure 1. Thermographic types of radiculopathy. Radiculopathy type(left) shows hypothermia along the nerve root distribution. Spot type(middle) shows localized hypothermia on pain area. Nonspecific type shows no specific thermal difference or abnormal temperature change.

L5 thermatomes

S1 thermatomes

Figure 2. Schematic drawing of L5(upper) and S1(lower) root thermatome.

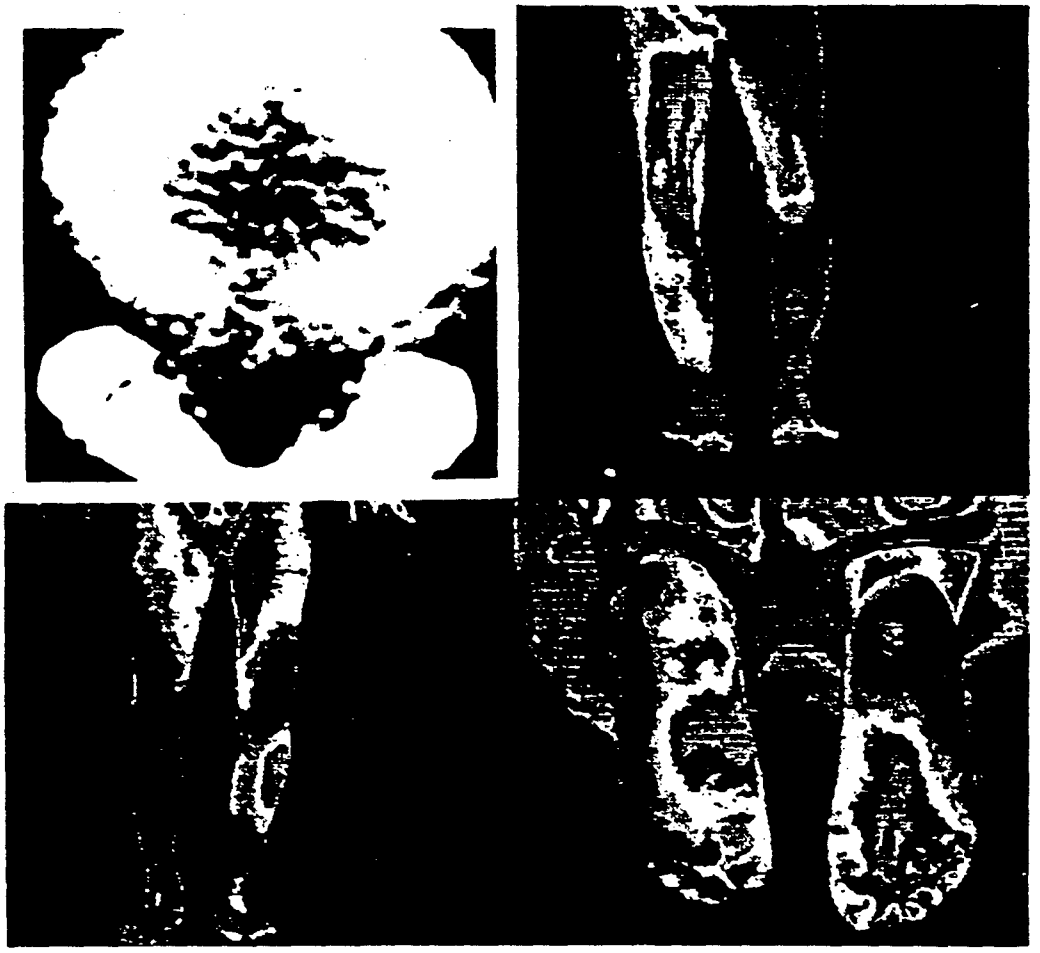

Figure 3. Thermographic change on L 4/5 disc herniation. Hypothermia is noted at buttock and posterior thigh with extension to anterolateral aspect of shin, dorsum of foot, medial aspect of sole.

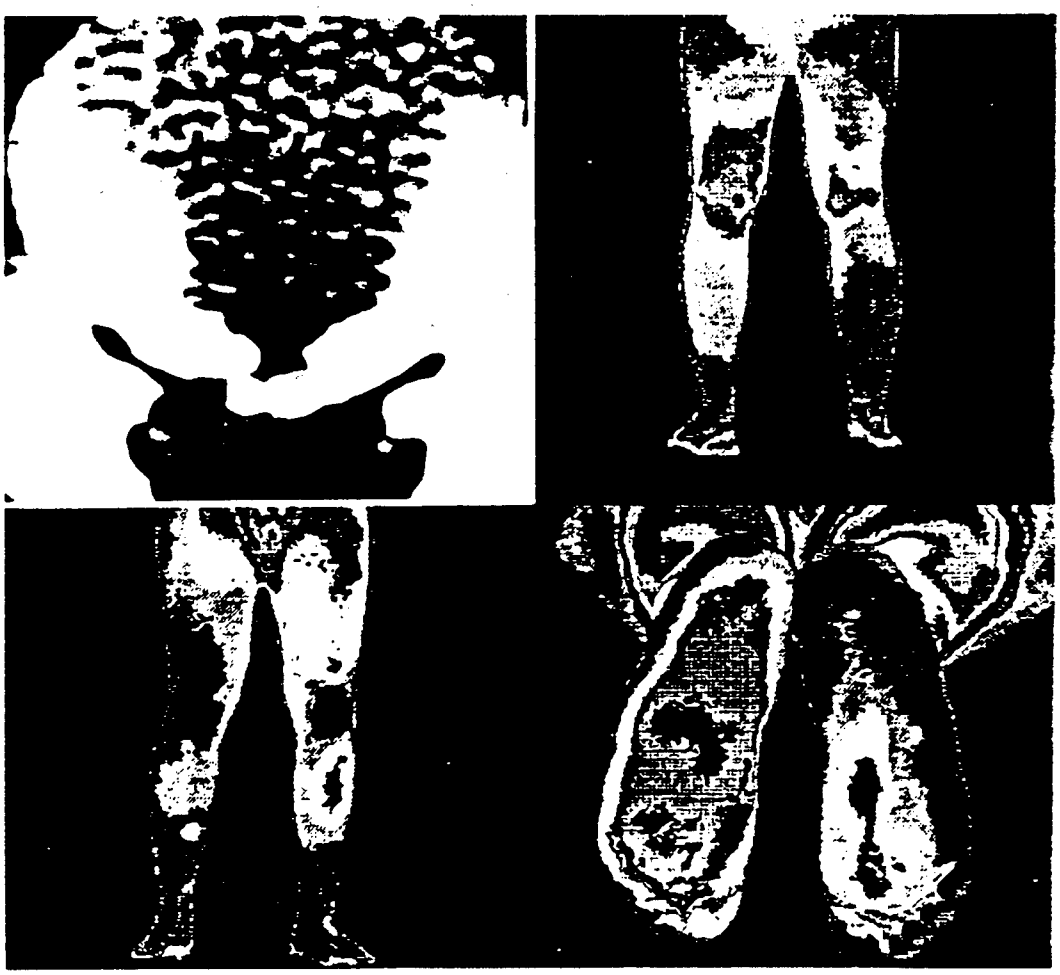

Figure 4. Thermographic changes in L5/S1 disc herniation. Hypothermia is noted on lateral aspect of buttock and thigh with extension to heel and lateral aspect of shin and sole.

L3 thermatomes

L4 thermatomes

Figure 5. Schematic drawing of L3(upper) and L4(lower) root thermatomes.

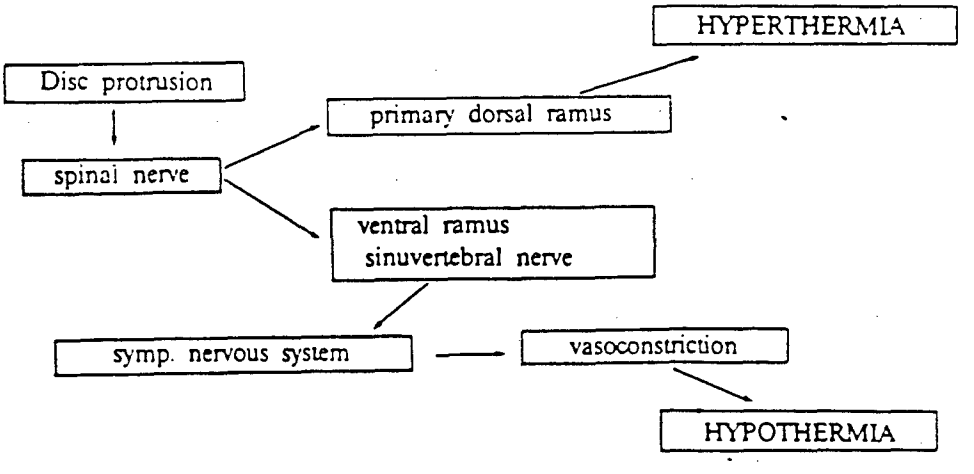

Figure 6. Mechanisms of thermographic change in disc herniation. Hyperthermia on anatomical level is presented by primary dorsal ramus of spinal nerve. The ventral ramus of spinal nerve causes vasoconstriction and hypothermia at the area of nerve innervation under the sympathetic nervous system via sinuvertebral nerve.

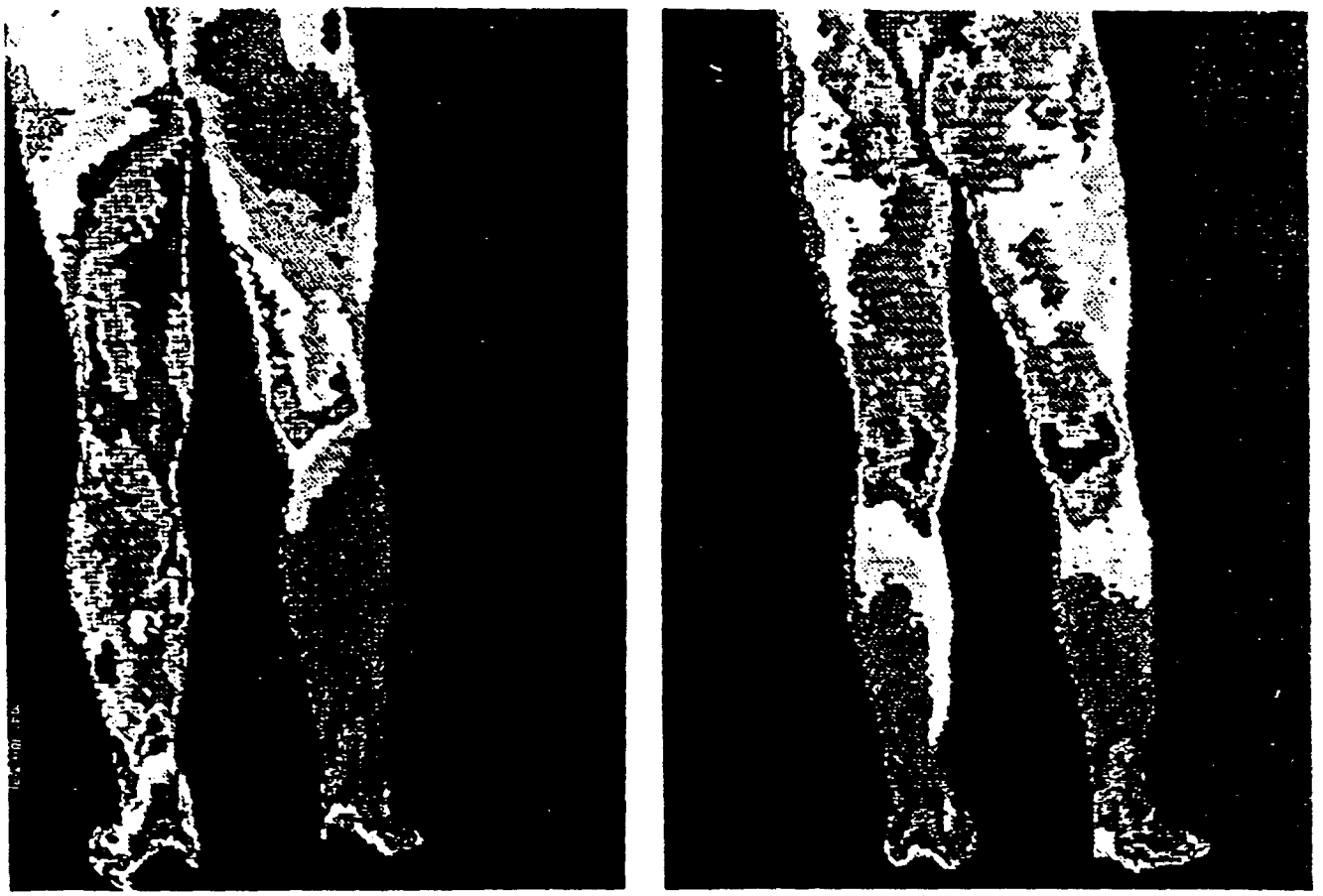

Figure 7. Thermographic change in pre- and postchemonucleolysis on L4/5 disc herniation. Preoperative severe hypothermiaon right leg(left) is normalized after chemonucleolysis(right).

Figure 8. Thermographic findings in pre- and postlaminectomy state of L4/5 dic herniation. Preoperative marked hypothermia on left anterior and posterior leg(upper) is changed to normal temperature after laminectomy(lower).

QUANTITATIVE THERMAL IMAGING IN RHEUMATOLOGY

Prof. Francis Ring
Royal National Hospital for Rheumatic Diseases
Bath BA1 1RL. U.K.

ABSTRACT

Inflammatory Joint Diseases, generally referred to as 'arthritis', are commonly indicated by increased temperature. Modern rheumatology now recognises a wide range of diseases and syndromes, which require completely different methods of treatment.

Heat is one of the oldest clinical signs of inflammation, and is efficiently recorded by infra red imaging techniques. Peripheral joints of the upper and lower limbs, e.g. knees, ankles, elbows and fingers, are subject to large changes in temperature from inflammatory conditions, i.e. up to 5°C. They are easily identified when the subject is examined in an ambient of 20°C, when the normal skin surface cools, increasing the temperature contrast from the persistent hot areas.

Standardisation protocols are used to derive a thermal index T.I. from a region of interest in the thermal image.

We have shown that anti inflammatory treatment will reduce this index to near normal levels (from 7.0 to 2.0), while analgesic (pain receiving agents) will not. Since many clinical tests for arthritis show improvement after pain relief, the T.I. is a valuable objective additional test to show the effectiveness of a drug treatment. Controlled trials of steroid injection and oral non-steroid drugs have been conducted with this standardised technique.

In Paget's Disease, Osteitis Deformans, diseased bone near the skin surface can be used to monitor the required drug treatment using Calcitonin and newer drugs such as Bisphosphonates. The latter is used in intermittent treatment, so the T.I. can indicate the optimum time for starting and stopping an individual course of the drug in difficult cases. Present day Thermal Imaging systems are reliable, and used under standardised conditions provide objective data for clinical trials in arthritis and locomotor diseases.

Key Words: thermal imaging, rheumatology, drug trials, Raynaud's Phenomenon, Reflex Sympathetic Dystrophy (R.S.D.), Paget's disease.

INTRODUCTION

Rheumatology embraces a spectrum of diseases, most of which affect the locomotor system. Arthritis is a general term which describes articular joint inflammation. During the inflammatory process the synovial membrane which supplies lubricant to the joint becomes thickened and increased blood supply increases the temperature. In other diseases, such as scleroderma the circulatory system in the extremities undergoes many changes, but blood supply is reduced. These and other rheumatic diseases result in localised changes in temperature.

Since the very early days of medicine, heat has been a classical sign of inflammation. The ability to record body heat was not achieved until the development of the thermometer in the 16 - 17th century. Even then, it took many years for physicians to apply measurement of temperature to their patients. One of the great pioneers in this progressive development was Dr Carl Wunderlich in Leipzig, Germany in the late nineteenth century.

Studies of skin temperature and thermal physiology have been hampered by the lack of efficient instrumentation. Medical textbooks still refer to laboratory experiments in which multiple thermocouples have been taped to the skin, and complex chart recording used to document the temperature data. It is not surprising therefore that the medical use and understanding of body temperature has progressed little from the clinical thermometer, which is essentially a maximum contact thermometer.

Infra red imaging is ideally suited to the study of skin temperature, because the human epidermis has a high emissivity (around 0.97). This was noted by Hardy, an American physiologist in 1934 [1]. Sixty years later, with more sophisticated technology and greater knowledge of physiology, we still agree with these data. Critics of thermal imaging point out that the technique only records the skin temperature. This often stems from a limited and sometimes outdated understanding of thermal physiology, still taught from the background of thermocouple recordings in elaborate laboratory settings. Technical advances in thermal imaging, particularly since the addition of image processing techniques have revolutionised the study of skin temperature. We now know much more about thermoregulation in man, and the effects of extremes of hot and cold environment [2]. When inflammation occurs in deeper tissues and joints, the skin will under the right conditions show an altered thermal behaviour. This means that normal control subjects can be used to establish a healthy baseline, from which patients with known disease can be compared. This has been achieved in rheumatology, and good international agreement reached over the application of thermal imaging [3].

Since the early days of thermal imaging and its use in medical research, a number of comparative studies have shown that the temperature over an inflamed joint is directly related to its inflammatory state. Comparisons have been made with Radionuclide markers and needle thermocouples inserted in to the joint. The results have shown that the increased blood flow and temperature within the joint relates

to that measured by radiometry when the skin has been cooled in a suitable environment. Biochemical indicators of inflammation also relate to these changes, so that sequential thermal images can be used to document the progress of disease, and its response, or lack of response to treatment [4]. One of the great virtues of this technique is that it is objective and non-invasive. This means that when the examination of a patient is difficult, e.g. dealing with young children or psychosomatic illness, thermal imaging is particularly useful. In many cases, the technique is not essential to diagnosis. However, in rheumatology, monitoring of disease progress is a major concern. In a disease with no known cure, drug treatment has to be rigorously assessed. In rheumatic diseases this is not a simple process. This is borne out by the extensive literature on the subject and the large number of available tests. No one single test adequately reflects the complex changes which occur in the whole patient with an inflammatory arthritis.

Drug trials have provided the greatest impetus to systematic monitoring of these diseases. In most cases a battery of tests are used to measure pain, joint tenderness and joint function. The patient's own preference for a drug and the 'hands on' measurements by a nurse or doctor are subjective, and strongly influenced by mental state. Even the relationship between the patient and the trialist will have a significant effect on the results. A placebo drug or treatment is commonly required, and the problems of placebo response in chronic diseases are well known. To the patient who has had all known treatments, the wonder drug is always around the corner, so a new preparation could be the one!

The need for objective and non-invasive monitoring of inflammation is therefore ideally met by quantitative thermal imaging. It is relatively simple and inexpensive, reproducible under the right conditions, and acceptable to the patient even when in pain.

Since 1958, work at The Royal National Hospital for Rheumatic Diseases in the U.K. has focused on improving methods for disease monitoring. Thermal imaging has proved to be a useful technique for a number of applications, and has been used extensively in clinical drug trials. The protocol for quantitative work has been developed over many years, and shows that a thermal index can be derived from a standard region of interest from an image. This index has a known normal range. Increase in this index occurs in inflammatory states, according to severity, and decreases with successful treatment [5,6]. Conversely, in conditions with reduced blood flow the index is below normal, and may indicate a return towards the normal after treatment with drugs which stimulate the circulation. These effects are more readily shown on the extremities, the arms and legs of a patient. In practice most affected joints can be monitored.

STANDARDISATION PROTOCOL

Optimal conditions for quantitative thermal imaging have been published, as consensus reports [7,8]. Our own technique which falls within these conditions establishes the following criteria.

1. Information is supplied to the patient prior to the test, to avoid major disturbances to the circulation, heart rate or skin condition. These include smoking, exercise, and ointments applied to the skin.
2. The patient is briefed, and then rested in a controlled ambient temperature for a fixed period prior to the test. Areas to be examined are unclothed, and legs and arms are stretched out, not crossed during this equilibrium period. A large chair with arms and a leg rest is ideal for this.
3. The imaging system is calibrated, to an external source if required, and allowed to run for a period to achieve full stabilisation. Investigations for inflammatory disorders are conducted in a 20°C ambient, but those associated with reduced circulation or investigations involving the vasomotor system are measured in an ambient of 23°C. These temperatures are suitable for extremities on human subjects in the U.K., but may vary at other latitudes and climatic conditions.
4. A series of standardised images are recorded keeping the field of view, distance, etc as standard. The digitised images are stored in a fixed temperature scale, routinely, 25°C - 35°C. Image processing allows the image to be optimised to show the thermal data in a specific part of the scan. However, the defined region of interest for measurement is unaffected by this display. A thermal index is calculated from each image and the result stored on the computer file. Our software allows us to store one or two indices from each image, which may be labelled Left or Right. We record both knees from the anterior view, but separately from the lateral. Both hands may also be recorded, from placing them on a board held across the chest. Elbows and ankles and other joints are recorded from a single image.
5. We report to the clinic or referring doctor within ten minutes having printed all images and their indices on an inkjet printer. The size of each image is less than 2 inches square, to speed reporting. However, when required for diagnostic purposes, larger thermal or photographic prints are supplied.

This procedure has an immediacy, which is useful in a busy hospital. The whole investigation may take less than 30 minutes, half of which time the patient has been resting, and the staff are not involved. When more elaborate procedures are used, and a series of images are recorded, this time may be extended to 45 minutes.

COLD STRESS TEST

A useful procedure for testing hands has been developed, which is primarily of value for quantifying Raynaud's Phenomenon. In this condition cold fingers and hands are experienced even in warm conditions. It is often associated

with other clinical conditions including Rheumatoid Arthritis. Our procedure uses a mild stress to the hands by immersion in water at 20°C for one minute. Experiment has shown that normal subjects recover from this cooling within ten minutes. Some normals show a reactive hyperaemia, where the fingers are hotter than the back of the hand for several minutes. This is a normal physiological response, when the brain sends a signal to the blood vessels in the fingers to dilate, increasing blood flow to achieve thermal recovery. In patients suffering from Raynaud's Phenomenon this does not occur. We therefore measure the mean temperature of the fingers, and subtract the mean temperature from the back of the hand to obtain a difference or gradient. This is close to zero in normals before stress, and may be similar or positive after stress. In Raynaud's phenomenon this gradient starts as a negative of some 2-3°C and becomes more negative after stress. We combine these two gradient values to from an index, which represents the response of the circulation in the hand to cold exposure. Increasing severity of disease is shown by increased negativity on this scale from +5 to -14°C [9]. This test has also proved of value in the diagnosis of Reflex Sympathetic Dystrophy. When one arm or hand is painful the initial thermal image may show only slight asymmetry of temperature. By the application of this test to both hands any deficiency in the autonomic nervous system will result in an inability to warm from cold stress. A number of centres, including our own have carried out studies to establish that the body is normally symmetrical in its temperature distribution. We therefore find that in using this cold stress test to the hands that in most subjects the result will be within 2°C on our index scale.

CLINICAL DRUG TRIALS

The use of corticosteroid injection into a joint is a long established procedure in rheumatology. There are a large number of preparations, resulting from many years of refinement to achieve a local and sustained treatment. A series of prednisolone analogues have been assessed in trials in Bath using the thermal index in controlled groups of patients. Each patient had both knees affected by arthritis, and one was injected with the steroid. Blood samples were taken to measure the steroid levels and thermal images to show the inflammatory state of both knees over three weeks following the injection. The results showed that the higher of the two doses of each drug tested produced higher blood levels and greater reduction in knee temperature. The larger molecule steroids were found to be more beneficial with slower increase in blood level, and more localised anti-inflammatory action. The uninjected knees also responded to the more soluble drugs due to their more systemic effect [10]. The temperature changes associated with local injection therapy are relatively large and obvious. Greater use is made in clinical medicine of oral drug therapy, and the effects may be less obvious to the clinician. Since inflammation can be chronic in arthritis, lasting over many years, a wide range of oral drugs are available. The rate of response to these oral non-steroid anti-inflammatory agents NSAID is much slower. The maximum effect may take several weeks to establish, and not all the NSAID's will operate at the same speed or dose. Our studies have shown that drugs which are analgesic, reducing pain, without reducing inflammation do not lower the raised thermal index. In fact, if the inflammation is active, this treatment will cause a rise in the index as the effects of the previous medication wear off. This action is used regularly in clinical trials as a washout procedure, prior to starting treatment with the test drug. The thermal index therefore gives an indication of the most actively inflamed joints, and provides a baseline from which to measure the change in temperature. In a number of clinical trials we have recorded the change in thermal index over a 14 or 21 day period. The fall in the index with successful treatment is found to be faster in the small joints of the hand, followed by elbow and ankle joints. Larger knee joints can take longer than 7 days to washout and more than 2 weeks to reach the maximal fall in temperature. These studies, were undertaken as double blind investigations, to objectify the anti-inflammatory effects of the drug regardless of pain relief [11]. Most of the clinical tests used are influenced by the level of pain. Since we know that a fall in temperature is proof of the anti-inflammatory effect, it is important to add thermal imaging to any trial of this category of drugs. By adapting our index to different regions of the body, we have been able to express the drug response as a compound index from several joints. The index is calculated using a constant baseline temperature obtained from large numbers of controls. By calculating the mean temperature from the region of interest defined for each anatomical region, this constant is easily determined. Thus, at 20°C ambient and under our own local conditions, a base factor of 26°C was taken for knees and ankle joints, and 28°C for hands and elbows. Thus an index of 2.00 from a knee, will be close to 28°C mean temperature, but close to 30°C for an elbow joint. However, we have shown that using this approach, the clinical staff are more able to judge the severity of inflammation without having to check on actual temperatures. It is also possible to combine these values if necessary so that the magnitude of change from treatment will be roughly equal.

These results have been published in peer reviewed journals, validated by independent investigating centres using the same technique. The same technique can also be used to measure the dose effect of a drug. Early work in Bath on animal models of inflammation has shown that pre-dosing the animals before inducing a local inflammation, with different strengths of the drug, gave graded relief from the inflammatory reaction. From this it was possible to plot a

dose response curve, and deduce an optimum dose for therapeutic effect. This is common practice in pharmaceutical development. Almost all of the tests used cannot be applied to humans, but in this case, thermal imaging and temperature measurement is equally applicable. We have conducted several dose finding studies on anti-inflammatory drugs as clinical trials. In one instance we were able to conduct an animal study on a new drug. Several years later the drug was released for human trials, when the optimum dose was established by thermal imaging inside three months [12].

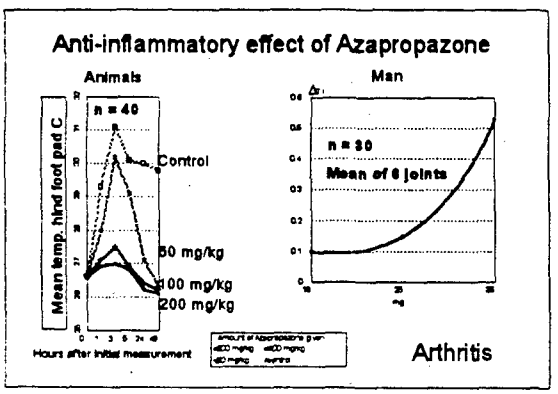

FIGURE: Temperature changes in experimental and human arthritis to test for the optimum dose of a new anti-inflammatory drug.

Legislation required that a large multicentred trial was carried out over a two year period. The findings of this study were in complete agreement with the thermal imaging study. In other areas in rheumatology this technique has been used for drug assessment. Paget's Disease of bone is relatively common in later life, but often undiagnosed. In a small percentage of patients, this becomes a serious and painful condition, with complications. It is necessary to treat the condition in these cases. For many years the drug of choice was calcitonin, given by daily injection. Major changes in the bone architecture occur in this disease, but develop very slowly. Heat and increased blood flow through the bone is a feature of the disease. We were able to measure the temperature distribution over sites on the body where bone lies close to the skin surface. The most obvious sites are the tibia and forehead, although the spine and forearm have been also measured with success. Variants of calcitonin, from biological and synthetic sources have all been tested, and shown measurable reduction of the index over the active sites. Other compounds, particularly bisphosphonates have emerged, which require a different pattern of treatment. Most of these compounds are used intermittently, because they are toxic if used regularly. Our studies have shown that the fall in temperature occurs more slowly than when calcitonin is used, and that the relapse of temperature can indicate when retreatment should commence [13].

Increasing interest is now being given to improved methods of drug delivery. Slow release capsules to reduce drug frequency and topical agents for transcutaneous delivery are all potential areas for this technique. We have tested one compound which is applied by an aerosol spray, and shown that the successful absorption of the anti-inflammatory agent depends on the vasodilation induced by nicotinic acid included in the formulation. Thermal imaging was used to plot the temperature increase over 15 minutes from application, and relate this to the blood levels of the drug sampled at regular intervals [14].

CONCLUSION

Thermal imaging has been successfully applied to clinical problems in rheumatology. It is of particular value in the assessment of drug treatment, although other forms of treatment can also apply. The growing interest in sports medicine and elite sport training brings other needs for objective monitoring of the locomotor system. Quantitative thermal imaging requires a strict protocol, but provides an inexpensive and objective tool for non-invasive investigation.

REFERENCES

1. J.D. Hardy, "The radiation of heat from the human body", *J Clin Invest*, Vol. 13, pp. 539-615, 1934.
2. Y. Houdas, E.F.J. Ring, "*Human body temperature: its measurement and regulation*", New York. Plenum. 1982.
3. E.F.J. Ring, D. Thomas, K. Ammer, J.M. Engel, "Thermal imaging in rheumatic and neuromuscular diseases", *European league against rheumatism EULAR bulletin*, Vol. 3, pp. 85-86, 1990.
4. P.A. Bacon, A.J. Collins, E.F.J. Ring, J.A.Cosh, "Thermography in the assessment of inflammatory arthritis", *Clinics in Rheumatic Diseases*, Vol. 2 no. 1, pp. 51-65, 1976.
5. A.J. Collins, E.F.J. Ring, J.A. Cosh, P.A. Bacon, "Quantitation of thermography in arthritis using multi-isothermal analysis. 1. The thermographic index", *Ann. Rheum. Dis.*, Vol. 33 no. 4, pp. 113-115, 1974.
6. E.F.J. Ring, "Quantitative thermal imaging", *Clin. Phys. Physiol. Meas.*, Vol. 11 suppl A, pp. 87-95, 1990.
7. J.M. Engel, J.A. Cosh, E.F.J. Ring, et al, "Thermography in locomotor diseases - recommended procedure", *Eur. J. Rheum. Inflamm.*, Vol. 2, pp. 299-306, 1979.
8. E.F.J. Ring, J.M. Engel, D.P. Page-Thomas, "Thermologic methods in clinical pharmacology", *Int. J. Clinical Pharmacology, Therapy and Toxicology*, Vol. 22 no. 1, pp. 20-24, 1984.

9. R.K. Will, E.F.J. Ring, A.K. Clarke, P.J. Maddison, "Infrared thermography: what is its place in rheumatology in the 1990s?", *British Journal of Rheumatology*, Vol. 31, pp. 337-344, 1992.
10. W. Esselinckx, P.A. Bacon, E.F.J.Ring, D. Crooke, A.J. Collins, D. Demmottaz, "A thermographic assessment of three intra articular predinsolone analogues given in rheumatoid arthritis", *B. J. Clin. Pharmacology*, Vol. 5, pp. 447-451, 1978.
11. P.A. Bacon, E.F.J. Ring, "Thermal imaging in assessment of drugs in rheumatology", *Recent Advances in Medical Thermology*, pp. 465-474, New York. Plenum. 1984.
12. E.F.J. Ring, "Thermal imaging and therapeutic drugs", *Biomedical Thermology*, pp. 463-474, New York. Alan Liss.1982.
13. E.F.J. Ring, J. Davies, "Thermal monitoring of Paget's disease of bone" *Thermology*, Vol. 3, pp. 167-172, 1990.
14. A.J. Collins, L.J. Notarianni, E.F.J. Ring, M.P. Seed, "Some observations on the pharmacology of 'Deep Heat' and tropical rubifacient", *Annals of the Rheumatic Diseases*, Vol. 43, pp. 411-415, 1984.

Clinical Infrared Thermal Image Testing: An Noninvasive Expression of Invisible Physiological Functions

IWAO FUJIMASA

Abstract–**At least four parameters involved in the determination of skin temperature need to be considered in the quantitative analysis i.e. location, time, environmental temperature and intrinsic physiological parameters. For the past two decades, many clinicians have pointed out the diagnostic ambiguity of thermographic pattern recognition. The ambiguity was mainly due to conversion from a six dimensional image to a two dimensinal image. Computer processing methods were therefore tested for thermography, and it proved theoretically possible to reduce the dimensions to permit the distinct display of an image of intrinsic thermal physiological function. I proposed eight fundamental thermo-physiological expressions named thermatomes and standardized diagnostic procedures using computed image processing. The software was applied to numerous cases, and has allowed the postulation of a standardized thermographic image diagnosis procedure.**

Keywords–**thermography, computer image processing, thermatome**

I. INTRODUCTION

CLINICAL INFRARED THERMOGRAPHY is a measuring method to make images of temperature distribution of the skin surface and a noninvasive analyzing tool of physiological functions that relate to skin temperature control. The imaging modality was named tele-thermography or infrared-thermography. We have called the measuring and analyzing methodology as thermology since around two decade that includes all phenomena relating temperature control of body and its environment.

The method is supported by a detector of infrared radiation and a pattern display that convert the infrared signals into temperature values. A principle of the measurement is obeyed the Stefan-Boltzmann's law: the radiated power of electromagnetic waves from a black body is proportional to the fourth power of the thermal dynamic temperature. The wave length of peak power ray that emitted from human body surface (around 30 °C) is 10 micrometer. After developing some far infrared detectors, we could measure the radiation from human body.

Hardy was the first scientist who measured far infrared radiation remotely in 1934 [1]. In 1937, Baird developed evapolograph, that was applied the thickness of oil membrane relating to the temperature, and displayed thermal patterns of surface from a long distance. Electronic detection of infrared radiating pattern was achieved by Lawson in 1957. He developed a liquid nitrogen cooled indium antimonide sensor and constructed an scanning image instrument [2]. As the first generation of commercially available thermographic instrument, liquid nitrogen cooled indium antimonide sensor (AGA, Sweden; Bofors, GB), non-cooled thermistor bolometer (Barnes, USA) [3] and liquid nitrogen cooled germanium gold sensor (Kobe-kogyo, Japan) [4] were installed in their scanners and made monochrome images on the CRTs. Many clinical trials had been done using these instruments and many clinical reports was published from the end of 1960s to 1980. The technology was rapidly prevailing clinical medicine.

The first clinical applications pointed to pattern recognition of abnormal thermal evidences. Subcutaneous or cutaneous tumor such as breast tumor and thyroid tumor, vascular disorder such as varicose vein, varicocele and arteriovenous fistula, and inflammation such as rheumatoid arthritis and other arthritis were easily detectable pathological status for thermographic diagnosis. However, the techniques of diagnosis depended upon detecting hot spots or cold spots that appear at the point of abnormal heat generation. The diagnosis was merely qualitative. One reason was that the thermograph in those day only indicated thermal distributions and did not express calibrated temperature values directly on the thermal images. Main streams of clinical thermology has stayed in pattern recognition until today in USA and Europe. However, the abnormal thermal pattern provoked by some pathological regions usually become more indistinct than that obtained from other imaging modalities that express their material characteristics. In order to compete against other imaging modalities in detecting physiological abnormalities, the quantification of thermal images became inevitable.

In 1975, a digitized imaging systems was announced by Fujitsu, and computerized thermography systems were prevailing in Japanese medical market [5,6]. In order to make a quantitative thermograph system, an application software for clinical thermal image handling named CTS: computed thermography system and an interface of on-line real time data processing were developed in 1985 [7]. The thermography obtained abilities expressing some pathophysiological functions using the computer systems. New targets of clinical thermography were generated. Peripheral vascular disorders,

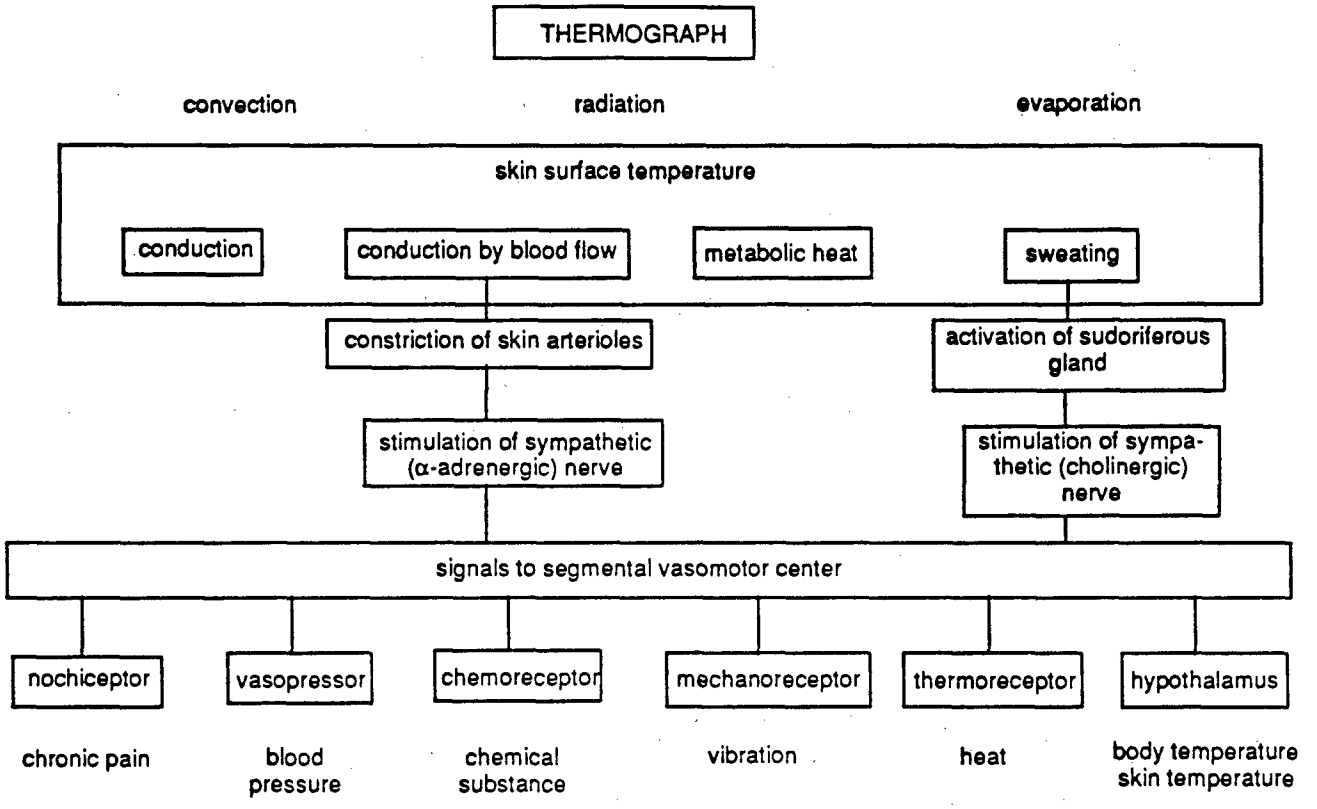

Fig. 1. Factors affecting skin temperature

neuro-musculo-skeletal diseases, autonomic nervous diseases and inflammatory diseases including local metabolic disorders could be analyzed quantitatively by the CTS. In 1982, health care insurance schema of Japan admitted to cover the thermography as thermal image testing [8].

II. THE KEY: ORIGIN OF ABNORMAL SKIN SURFACE TEMPERATURE DISTRIBUTION

Thermogram must be regarded as physiological information that include body temperature and the surface temperature. When thermograms are expressions of physiological functions determining temperature control, the thermo-physical background of the body systems must be taken into consideration. The situation is analogous to that in which many kinds of radiological image analyses are based upon the understanding of anatomical and structural knowledge of the human body. Under thermally neutral conditions, in which there is a stable equilibrium between the production and dissipation of heat within the body, it is possible to classify diagnostic criteria for the evaluation of thermograms based upon the understanding of numerous thermo-regulatory parameters, as shown in Fig. 1 [9].

In thermally neutral environment, the most direct parameter that influence upon skin temperature distribution is blood flow rate in the cutaneous tissue. We usually observe the distribution of skin blood flow rate at first glance. The local blood flow rate is controlled by vasomotor tones which constrict skin arterioles. Therefore, we can observe local abnormalities of autonomic nerve system especially α-adrenagic nerve system. As the vasomotor centers are distributed among segments of vertebral bones, we can also analyze segmental abnormality of temperature control. Many other physiological parameters affect directly or indirectly temperature distribution of skin surface. Thus, the eight parameters listed in Table I might be regarded as the most fundamental physiological criteria, and these have been utilized in the diagnosis of diseases.

TABLE I

1	Angio-thermatomes
2	Functional angio-thermatomes
3	Dermato-thermatomes
4	Myo-thermatomes
5	Metabolic-thermatomes
6	Dynamic thermatomes of low environmental temperature
7	Dynamic thermatomes of medication
8	Dynamic thermatomes of various kinds of stress

In Table I, I use a terminology named *thermatomes*. P. LeRoy proposed the new term *thermatome* to define the abnor-

TABLE II

Diseases	Diagnostic criteria and Techniques
Peripheral vascular diseases	Abnormal angio-thermatome
Local metabolic disorders	Hot or cold areas, metabolic-thermatome, thermographic-index
Chronic pain	Dermato-thermatome, myo-thermatome, angio-thermatome
Autonomic nerve system disorders	Dermato-thermatome, stress test
Inflammatory diseases	Hot area, metabolic-thermatome, thermographic index
Tumors	Hot or cold areas, metabolic-thermatome, abnormal vascular pattern
Body temperature abnormalities	Abnormal body temperature and discrepancy between skin and body temperature

mal infrared segmental pattern of thermography transmitted by somatosensory and sympathetic pathways [10]. I expand the definition that thermal images associated with the thermophysiological location are defined *thermatomes*. [11]. The summarized content of the eight fundamental thermophysiological procedures are:

1) Angio-thermatomes, in which the location depends on skin blood-flow distribution [12].
2) Functional angio-thermatomes, in which skin blood-flow distribution is controlled by adrenergic sympahtetic nerve stimulation [13].
3) Dermato-thermatomes, in which the thermal image distribution is influenced by the neuro-dermatome [8].
4) Myo-thermatomes, in which the thermal image distribution is similar to the muscular distribution [14].
5) Metabolic-thermatomes, in which hot or cold spots are produced by metabolic abnormalities of the skin and subcutaneous tissue [15].
6) Dynamic thermatomes, in which images are caused by exposure to low environmental temperature [16]
7) Dynamic termatomes, in which images are produced by the administration of medication [17].
8) Dynamic thermatomes, in which images are produced by exposure to various kinds of stress [18].

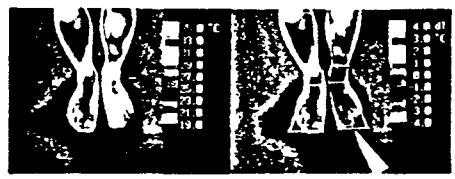

Fig. 2. An angio-thermatome of femoral artery obstraction
Left: standardized thermogram
Right: asymmetry detection thermogram

Fig. 3. A functional angio-thermatome of left-side Horner's syndrome by cervical syringomyelia

The pathophysiological condition is determined by carrying out a number of the above procedures and then performing a computer analysis of the result in practical clinical testings. Diseases for which thermographic techniques can be applied are listed in Table II.

III. EIGHT THERMATOMES: FUNDAMENTAL THERMO-PHYSIOLOGICAL IMAGE EXPRESSIONS

Angio-Thermatomes

The skin temperature distribution is determined primarily by the skin blood flow. Arterial obstruction usually causes a severe drop in the peripheral skin temperature in cool and neutral thermal environments. Typical thermographic images are obtained with arteriosclerotic obliterans (ASO) and thromboangitis obliterans (TAO) in the extremities. It is proposed that such images be called "*angio-thermatomes*", as they reflect the local blood flow distribution. However, it must be stressed that the name is not based on the original concept of the angiosome, which is derived from the source arteries of the body used in skin flap transplantation [12].

Fig. 2 shows a low temperature area on the left foot caused by obstruction of the left femoral artery. The assymetry detection thermogram (shown in the right side thermogram in Fig. 2) shows a low temperature area of 3°C on the left foot caused by low blood flow and a high temperature area of 2°C on the lower leg caused bypass flow on the skin.

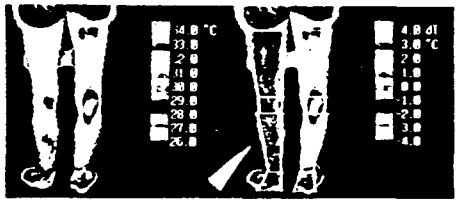

Fig. 4. A dermato-thermatome of a case of L5/S1 lumbar disk herniation. Left: standardized thermograph; right: asymmetry detection thermogram.

Functional Angio-thermatomes

The skin blood flow is controlled by the adrenaergic sympathetic nerve systems. In particular, the vasomotorial sympathetic nerves in the distal regions of the extremities are composed of only contractile nerve endings and these control the body temperature. When areas of low temperature are observed in an extremity, it is necessary to consider the cause of the lower temperature, for example, whether the vasomotor sympathetic nerve has been excessively stimulated. Lower temperature images are sometimes not produced as a result of the mechanical obstruction of peripheral arteries but are due to functional obstructions, such as occurs in case of Raynaud's syndrome. Many of these patients only exhibit low skin temperatures in their fingers when under stress or in a cool environment, since it is such stress that causes contraction of their peripheral arteries. When higher temperatures are observed on the extremities or on the face, this may indicate a lack of sympathetic stimulation in those regions. The term "*functional angio-thermatome*" indicates that the lower or higher temperature areas are a reflection of functionally reduced or increased blood flow, respectively.

In Fig. 3, the left half of the body is at a higher temperature than the right. The patient suffered from cervical syringomyelia and shows left-side Horner's syndrome. The pattern indicates a lack of sympathetic control in the left half of the body, and resembles a thermogram of stellate ganglion block.

Dermato-thermatomes

The sensory nerve are distributed at the segment of vertebral level, with the segment referred to as a "*sensory dermatome*". Because the vasomotor centers of the vertebrate are present in each somatic segment, the skin temperature is expected to be distributed within the segments, which are usually called "*thermatomes*". Here, they are referred to as *dermato-thermatomes*, i.e. thermally expressed sensory dermatomes. The terms are usually used with regard to the lower temperature regions produced as a result of radiculopathy. The sensory segment of skin exhibiting chronic pain coincides with the lower temperature area of the extremities (especilally legs and feet).

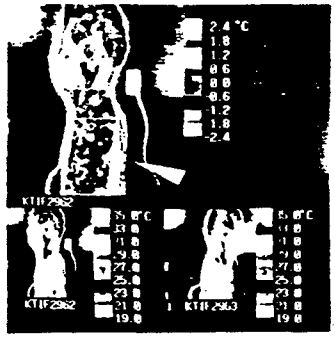

Fig. 5. A myo-thermatome of a left deltoid muscle lesion accompanied by chronic pain. Upper: asymmetry detection thermogram; lower two: standardized thermograms of left and right shoulders.

Fig. 4 shows a case of L5/S1 lumbar disk herniation. The skin temperature of the posterior area of the left leg and the surface of the Achilles' tendon is 1° to 2°C lower than that of the right (the left thermogram is an asymmetry detection thermogram). The area of pain coincided with the area of lower temperature indicated by the L5/S1 sensory dermatome. It has been agreed that the area of chronic radiculopathic pain coincides with the lower temperature regions and that the dermato-thermatome is a good screening tool for the detection of radiculopathic complaints. Many explanations for the relationship between low temperature and pain have been proposed, but the situation is as yet unclarified.

Myo-thermatome

Recent research has shown that the low temperature areas can indicate muscular lesions. In particular, areas of low temperature skin on the surfaces of the body trunk and the central side of the extremities may indicate a reduced blood flow or the lower temperature of a muscle under the skin. Low temperature zones produced as a result of whiplash injury or cervical radiculopathy indicate the muscle lesion directly. The *myo-thermatome* is defined as a thermogram expressing muscle lesions.

Fig. 5 shows a left deltoid muscle lesion accompanied by chronic pain. The upper thermogram was obtained by subtracting the lower right thermogram from the left. The regions observed to be at a lower temperature (0.6 ~ 1.8°C) were found to coincide with the area of pain and deltoid muscle. This is also an example of an asymmetry detection thermogram.

The control mechanisms involved in determining skin temperature on the trunk and central paths of the extremities are still unknown. However, it is certain that the blood flow is not related to the control of body temperature but is regulated by a sympathetic pseudomotor or the cholinergic system.

Metabolic thermatome

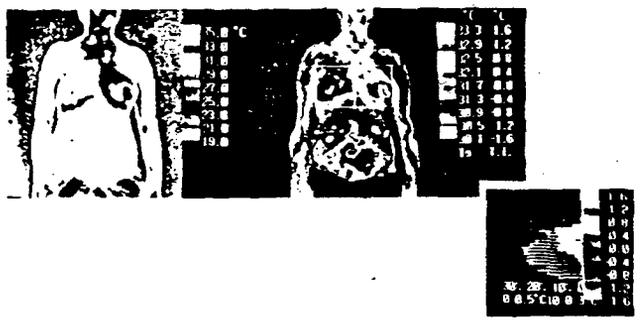

Fig. 6. A dynamic thermatome shows a case of early stage left breast cancer detection due to dynamic skin temperature change in cool environmental temperature. Left: standardized thermogram; mid: sequential subtraction thermogram; right: histograms of ROIs.

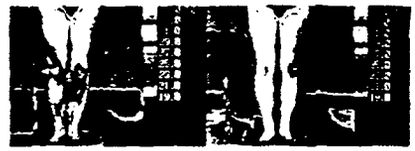

Fig. 7. Dynamic thermatomes of the effect of eperison chloride on the skin blood flow in the legs of a patient suffering from an L5/S1 lumbar disk hernia. Thermograms: standardized thermograms.

Thermographic observation can detect abnormal temperature distribution. Many thermographers consider that hot or cold spots indicate metabolic abnormality, and the detection and measurement of hot spots are still an important method in the differential diagnosis of tumors and for making prognoses for inflammatory disease. The term "*metabolic thermatomes*" refers to a metabolically dominant thermal image. However, the metabolic image is usually combined with the skin blood flow image, which may lead to ambiguity. A thermal stress test is therefore required in order to distinguish between the two.

Dynamic thermatome expression due to exposure to low environmental temperature

The physiological procedures described above can be performed when a thermal equilibrium exists with the environmental temperature. The equilibrium condition is called the thermally neutral condition, and exists at 29° - 31°C when in the nude and at 25° - 29°C when light clothes are worn. In winter, very low temperaure of the skin of the extremities are frequently experienced, and temperature acclimatization may require more than 30 minutes. As the tension of the sympathetic nerve system usually increases in winter, care must be taken with diagnoses of peripheral vascular disease unless sufficient thermal acclimatization has been allowed.

Under thermal non-equilibrium conditions, the dynamic thermal condition process can be observed on the skin. The

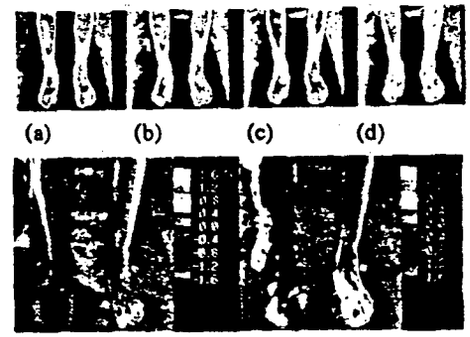

Fig. 8. Dynamic thermatomes shows the sequential thermal images and subtraction thermograms of legs suffering from ASO (right leg). Upper images: sequential standardized thermograms; lower images: sequential subtraction thermograms.

local cooling stress method is useful for the detection of such metabolic abnormalities as tumors and inflammation. Fig. 6 show a case of early stage left breast cancer detection due to dynamic skin temperature change. The thermogram on the right is a time subtraction image obtained from two thermal non-equilibrium observations. Comparison of these shows that the temperature of the hot spot in the lower left quadrant of the left breast remained unchanged, showing that the hot spot exhibits a strong temperature inertia in a cool environment. This phenomenon indicates the possible existence of arteriovenous fistra, which is produced by breast cancer, and the skin temperature indicates the deep body temperature directly.

Dynamic thermatome expression due to the application of drugs

Observation of the thermographic changes following the administration of a vasodilator, muscle relaxant, or antiphlogistic agent, etcetra, allows evaluation of the dynamic effects of the drugs on skin blood flow. If the action of a drug on the temperature regulation mechanism is known, the drug can be used for stress testing.

Even if the thermological action of a drug is unknown, itis easy to evaluate the effects of the drug. Fig. 7 shows the effect of eperison chloride on the skin blood flow in the legs of a patient suffering from L5/S1 lumbar disk hernia. The left thermogram was obtained prior to administration of the drug, and the right thermogram obtained following administration. The skin temperature of the legs was markedly increased and the pain was diminished.

Dynamic thermatome expression due to various kinds of stress

Dynamic changes in skin temperature caused by thermal, mechanical, chemical and psychological stresses have been analyzed. Post-ischemic reactive hyperemia caused by arterial occlusion have been analyzed quantitatively and graphically in the extremities suffering from TAO and ASO. Fig. 8 shows (from left to right in the upper row) the sequential thermal im-

TABLE III

1.	Standardized thermograms
2.	Asymmetry detection thermograms
3.	Sequential subtraction thermograms
	A. Subtraction between two thermograms
	B. Differential thermograms
	C. Secondary differential thermograms
4.	Thermographic index thermograms
5.	Skin blood flow rate images
6.	Thermal rhythm spectrography
7.	Ordinal image handling tools

TABLE IV

Step 1. Standardized thermograms
(Screening for abnormal temperature distribution)
Step 2. Precise thermograms with temperature analysis of region of interest (ROI)
(Precise temperature analysis of ROI)
Step 3. Asymmetry detection thermograms
(Detection of true abnormal regions)
Step 4. Thermographic index thermograms (TI) and TI histograms of ROI
(Determination of the degree of heat accumulation)
Step 5. Sequential subtraction thermograms
(Analysis of the thermal dynamics of ROI)

ages of legs suffering from ASO (right leg) which were taken (a) before obstruction, (b) directly after 3 minutes' obstruction of the light thigh, (c) 3 minutes after release, and (d) 6 minutes after release. The lower left thermogram is a subtracted image obtained by subtracting (a) from (b), and shows the temperature decrease on the right foot and the increase on the left toes. The lower right thermogram was obtained by subtracting (b) from (c). As the first right toe did not show an increase in skin temperature, the artery of the toe might have become structurally obstructed. The left foot temperature increased reactively.

When stress is applied, it should not be applied to that part which is under examination. Quantitative analyses were not performed on the effects of stress on different parts of the body.

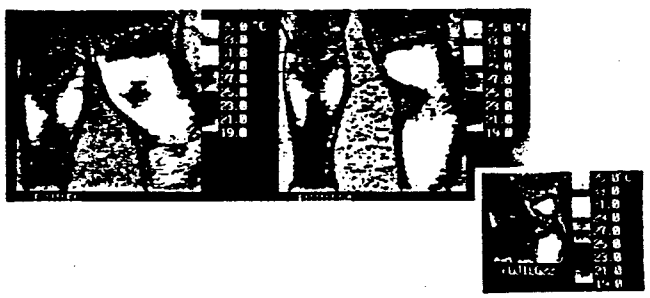

Fig. 9. Step 1: Standardized thermograms

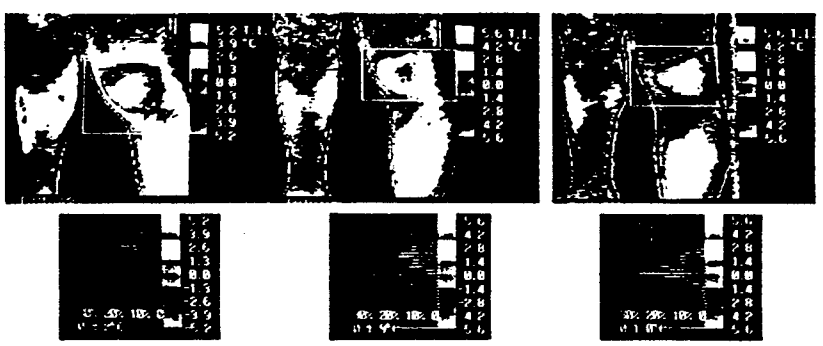

Fig. 10. Step 2: Precise thermograms with temperature analysis of region of interest (ROI)

IV. DIAGNOSTIC PROCEDURES

Thermographic image processing functions

Computed thermography systems (CTS) have been developed for the quantitative evaluation of thermograms. The image processing functions are classified in Table III. The four most fundamental functions can be summarized as follows:

Standardized thermograms show the temperature with a fixed color coded image and are used for screening abnormal hot or cold areas on the skin. The recommended temperature ranges ar 19° - 35°C or 26° - 35°C.

Asymmetry detection thermograms are obtained by the subtraction of the skin temperature of one side of the body of the other. The diagnostic basis of the thermogram depends on the symmetrical distribution of skin temperature about the sagittal plane [19]. The temperature difference between the two sides of the body is frequently an indication of an abnormal angiothermatome, dermato-thermatome, myo-thermatome or metabolic thermatome.

Sequential subtraction thermograms are obtained by the subtraction of two sequentially taken thermograms, and allow the display and quantification of dynamic temperature changes.

Thermographic index thermograms show the differnce between the temperature in one area of the body and the temperature at a standard point of the body. They permit an estimation of the extent of inflammatory metabolic heat accumulation, and allow elimination of individual and seasonal variations from a thermogram.

Diagnostic procedures using computed thermograms

Using above mentioned concepts and image processing tools, we can set up standardized diagnostic procedures. A five-step procedure is proposed for thermographic diagnosis

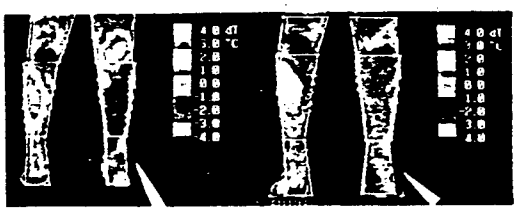

Fig. 11. Step 3: Asymmetry detection thermograms

Fig. 12. Step 4: Thermographic index thermograms (TI) and TI histogramsof ROI

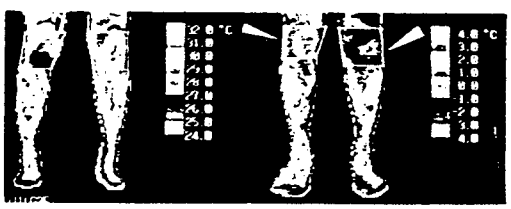

Fig. 13. Step 5: Sequential subtraction thermograms

(see Table IV). The thermographic diagnosis procedure is explained for a case of osteoarthropathy (see Figs. 9 to 13).

In *step 1*, standardized thermograms are taken of abnormal temperature regions. In the three thermograms in Fig. 9, the left image indicates a high temperature on the left knee at the onset of osteoarthropathy; the high temperature zone of the inflammation gradually diminishes in the middle image (3 days after onset) and the right image (7 days after onset). The standardized thermogram taken in the range 19° to 35°C can be used for the screening of abnormal temperature regions. The environmental temperature is indicated by the area of the thermogram corresponding to the area behind the patient.

In *step 2*, precise observations of the region of interest (ROI) are performed (see Fig. 10). Enlarged thermograms covering a narrow temperature range, temperature analyses of the ROI, and histograms are compared sequentially as the disease progress. Fig 10 shows the temperature differnce between the 1 st and 7 th days of the disease.

In *step 3*, the asymmetry detection thermograms are processed. The abnormal temperature regions are clearly defined following the elimination of individual background thermal patterns. In Fig. 11, the temperature of the right leg was subtracted from that of the left leg, and superimposed on the left leg. The left thermogram (taken on day 1) indicates the inflammation lesion and the existence of a low temperature area on the lower leg. The right thermogram (7th day) shows the slight inflammation on the upper left corner of the knee.

In *step 4*, the thermographic index thermograms are processed, and give quantitative information concerning abnormal heat accumulation or heat loss as the disease progress, thereby allowing easy evaluation of the therapy and permitting a prognosis for the disease to be made. The histograms in Fig. 12 show a rapid decrease in the thermographic index (TI) from 3.2° to 1.0°C.

In *step 5*, a sequential subtraction thermogram is utilized. In Fig. 13, the ROIs of the left thermogram (taken on the 1st day) are subtracted from those of the right thermogram (7th day) and displayed on the corresponding ROI of the right thermogram. It is clear that although the right knee temperature did not change within the 7 days, the left knee temperature decreased by about 3°C.

The above five-step procedure can be followed with almost all thermographic testing, although it is possible that the steps may have to be varied to accomodate certain special pathophysiological conditions.

V. CONCLUSIONS

At least four parameters involved in the determination of skin temperature need to be considered in the quantitative analysis i.e. location, time, environmental temperature and intrinsic physiological parameters. For the past two decades, many clinicians have pointed out the diagnostic ambiguity of thermographic pattern recognition. The ambiguity was mainly due to conversion from a six dimensional image to a two dimensinal image. Computer processing methods were therefore tested for thermography, and it proved theoretically possible to reduce the dimensions to permit the distinct display of an image of intrinsic thermal physiological function. The software was applied to numerous cases, and has allowed the postulation of a standardized thermographic image diagnosis procedure.

However, this standardized diagnostic procedure must be further developed if the use of thermography in medicine is to be expanded. It can be concluded that computer image processing is indispensable in the quantitative evaluation of thermographic images.

REFERENCES

[1] J.D. Hardy, "The Radiation of Heat from the Human Body," *J. Clin. Invest.* vol. 13, 593-604, 605-614, p. 615-624, 1934

[2] R.N. Lawson, "Thermography - a New Tool in the Investigation of Breast Lesions," *Canadian Services Med. J.*, vol.13, p. 517-524, 1957

[3] Gershon-Cohen and R.B. Barnes, "Thermography and its Clinical Application," *Ann. N. Y. Acad. Sci.*, vol. 121, no. 1, p. 304, 1964

[4] I. Fujimasa, Y. Sakurai and K. Atsumi, "Some Physical and Physiological Aspects of Thermography," *Medical Thermography*. Univ. of

Tokyo Press: Tokyo, 1973, p. 31-61

[5] I. Fujimasa, Y. Kajiyama, M. Iwatani and K. Atsumi, "Microprocessor Processed Human Thermographic Images," *MEDINFO-83*. IFIP-IMIA, North-Holland: Amsterdam, 1983, p. 393-396

[6] I. Fujimasa, "Development and Clinical Application of the Integrated Thermal Image Analysis System (IMTIAS)," *Medical Thermology*. Sheridan Press: Washington, DC., 1986, p. 299-301

[7] I. Fujimasa, M. Nakajima, K. Mabuchi, T. Chinzei, Y. Abe, Y. Hyakuna and K. Atsumi, "Development of an On-line Real-time Computed Thermography System (CTS)," *MEDINFO-86*. Elsevier Science Pub: New York, 1986, p. 709-711

[8] I. Fujimasa, Ed. *Physiological Function Imaging: Thermography*. Syujyun-sha: Tokyo, 1988, pp. 227

[9] I. Fujimasa, "Pathophysiological Understanding of Thermograms," *Physiological Function Imaging: Thermography*. Syujyun-sha: Tokyo, 1988, p. 36-39

[10] P.L. LeRoy, W.M. Bruner, C.R. Christian, R. Filasky and S. LeRoy, "Thermography as a Diagnostic Aid in the Management of Chronic Pain," *Evaluation and Treatment of Chronic Pain*. Urban & Schwarzenberg: Baltimore, 1985, p. 231-250

[11] Y. Miki and I. Fujimasa, "Symposium on Pathophysiological Mechanism of Abnormal Body Surface Temperature," *Biomedical Thermology*, vol. 9, no. 2, p. 281-313, 1989

[12] G.I. Taylor and J.H. Palmer, "The Vascular Territories (Angiosomes) of the Body: Experimental Study and Clinical Applications," *British J. of Plastic Surgery*, vol. 40, no.2, p.113-141, 1987

[13] M. Iriki, "Physiology for Understanding the Body Surface Temperature Distribution," *Physiological Function Imaging: Thermography*. Syujyun-sha: Tokyo, 1988, p. 13-19

[14] K. Motomura, K. Mabuchi, T. Chinzei, Y. Abe, I. Fujimasa and K. Atsumi, "Thermography of Neuro-muscle-skeletal Systems," *Physiological Function Imaging: Thermography*. Syujyun-sha: Tokyo, 1988, p. 103-106

[15] E.F.J. Ring, "Objective Measuement of Arthritis by Thermography," *Acta Thermographica*, vol. 5, p. 14-18, 1980

[16] I. Fujimasa, K. Imachi, K. Mabuchi, T. Chinzei, Y. Abe and K. Atsumi, "What Kind of Physiological Functions are Possible to Convert into Graphic Patterns from Thermal Images," *Biomedical Thermology*, vol. 7, no. 1, p. 56-58, 1987

[17] K. Motomura, K. Mabuchi, T. Chinzei, Y. Abe, I. Fujimasa and K. Atumi, "Thermographic Evaluation of Drug Effects," *Physiological Function Imaging: Thermography*. Syujyun-sha: Tokyo, 1988, p. 199-203

[18] I. Fujimasa and T. Chinzei, "Dynamic Thermographic Analysis System at Stress Testing," Proc. of 12th Intern. Conf of IEEE EMBS, p. 1582-1583, 1990

[19] S. Uematsu, "Skin Temperature Measurement: a Clinical Perspective," *Biomedical Thermology*, vol. 11, no. 4, p. 256-268, 1991

Low-Cost Uncooled Thermal Imaging

Charles Hanson and Bill Stearns

Texas Instruments, Inc.
P.O. Box 655012, MS 37
Dallas, TX 75265

The cost of thermal imaging systems has long been the principle barrier to its use for non-military applications. Texas Instruments (TI) has developed a new technology and a new class of thermal imaging systems that are substantially simpler and lower in cost than conventional devices. TI is continuing development of technology and systems for military applications, and is teamed with Hughes to develop and produce systems for commercial use. A sensor for mounting on police cruisers is currently available. Planned systems include surveillance cameras, night driving aids and handheld, portable models.

Key words:
Thermography, thermal imaging, infrared

Introduction

All objects emit infrared radiation. The intensity and spectrial distribution of the radiation depend upon the temperature of the object and the condition of its surface. Figure 1 shows the spectral distribution of radiation from perfect surfaces at several different temperatures.

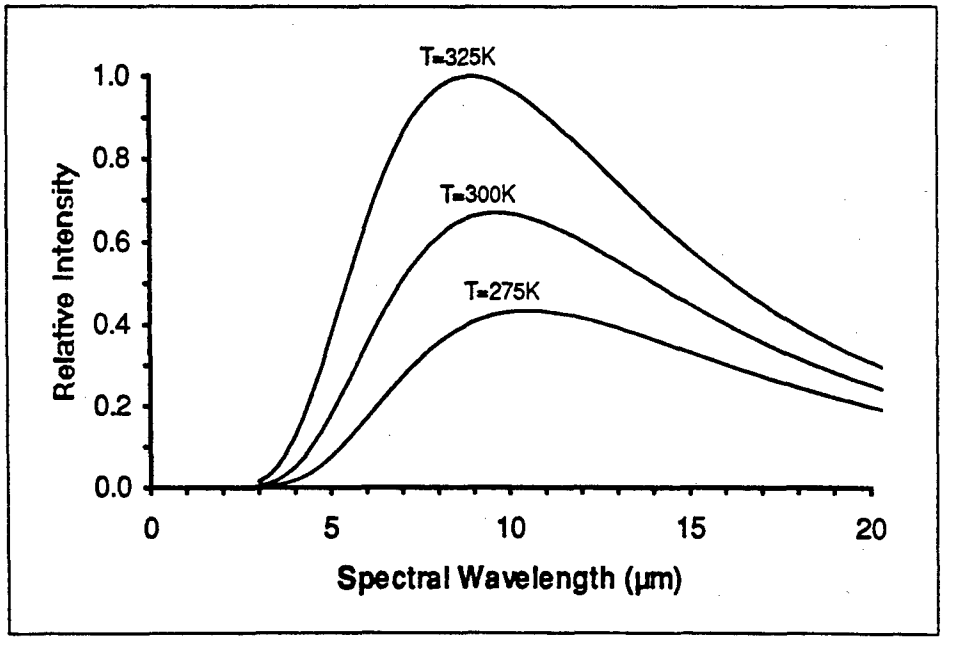

Figure 1 - Spectral emission of radiation from perfect surfaces at various temperatures.

In the past thermal imaging systems have been based upon photon detectors, which produce electrical signals as the direct result of absorption of IR radiation. Photon detectors are highly sensitive, but they are expensive to produce, require cryogenic cooling, and often require opto-mechanical scanning. TI's new uncooled detector technology is based upon thermal detectors, which produce electrical signals as the result of temperature changes that occur when the detector absorbs IR radiation. When an element absorbs IR radiation, it converts the energy to

heat, which results in an increase in the temperature of the detector. The detector elements are fabricated so as to be thermally isolated from each other and from their surroundings in order to maximize the temperature change for a given amount of absorbed energy. The detector elements are made from a material that has an electrical property that is extremely sensitive to temperature. By measuring that property one can detect the presence of IR radiation.

Although a thermal detector is typically less sensitive than a photon detector, it has many advantages. Its spectral response is determined only by the characteristics of an absorbing layer and not by the thermally sensitive material itself. This permits tuning the response to achieve virtually any desired spectral response, including very broad band response. Thermal detectors are significantly less expensive to fabricate than thermal detectors, and they require neither cryogenic cooling nor opto-mechanical scanning. This results in thermal imaging systems that are sufficiently sensitive for many applications and that are less expensive than conventional systems by nearly an order of magnitude.

Uncooled thermal imaging at Texas Instruments began in the mid-1970's and has evolved into a major activity addressing multiple military and commercial applications. For most of the development time the emphasis has been on systems for military applications, primarily small arms weapon sights. As performance improved potential military usefulness also improved, and important developments have included surveillance sights and night driving aids. As the technology has matured and stabilized, potential commercial markets have emerged. The commitment to serve these markets has led to the establishment of a growing production capability for both detectors and imaging system.

Technology Description

TI's uncooled detector arrays today consist of more than 80,000 pixels arranged in a 328 (horizontal) x 245 (vertical) matrix. The elements are positioned on 48.5 μm centers, with no space between them (*i.e.*, 100% fill factor). The basis of the technology is ceramic ferroelectric barium strontium titanate (BST) operating near its ferroelectric phase transition. Each detector element is a capacitor with BST as the dielectric. The dielectric constant of BST is extremely sensitive to temperature near the phase transition. When an electric field is applied to the capacitor, the charge on the capacitor is indicative of its temperature. Any change in temperature generates a current that is measured by an amplifier on an attached readout integrated circuit. The structure of the device is shown in Figure 2. The signals from the array of detector elements are multiplexed and read sequentially in a format that is compatible with television standards.

To achieve maximum temperature excursion when the detector elements are exposed to IR radiation, each element is thermally isolated from its surroundings. A polyimide mesa provides mechanical support for each element, and an over-the-edge metal pattern provides local electrical interconnection between the detector element and the readout IC beneath. The thickness and width of the metal are minimized to reduce the flow of heat between the IC and the detector elements. An indium metal bump is present on both the BST capacitor and the mesa, and the two are heated and pressed together to form a permanent bond.

The array of BST capacitors is reticulated to thermally isolate the pixels from one another. This reduces thermal spreading and improves the sharpness of the image. The IR absorbing coating consists of three layers that form a resonant cavity for absorption of IR radiation of the desired wavelengths. The resonance is broad, and average absorption over the 7.5 μm to 13.0 μm band is typically greater than 95%. The thermal characteristics of this coating are controlled to further minimize thermal spreading.

The system consists of an IR objective lens, a chopper, a detector array, a single electronic circuit board, and a display. Because there is no opto-mechanical scanner the IR objective lens is simple, usually consisting of no more than three optical elements. Some system designs permit use of interchangeable lenses, much like a 35-mm camera. A small, simple mechanical chopper modulates the flow of IR radiation into the detector array. This greatly simplifies the electronic design for only a small penalty in mechanical complexity. The electronics processor digitizes the signals from the detector array, processes the results, converts the data to an analog stream, and adds the appropriate timing signals for compatibility with standard NTSC television. Power dissipation is minimal and operation is quite because there is no need for cryogenic cooling.

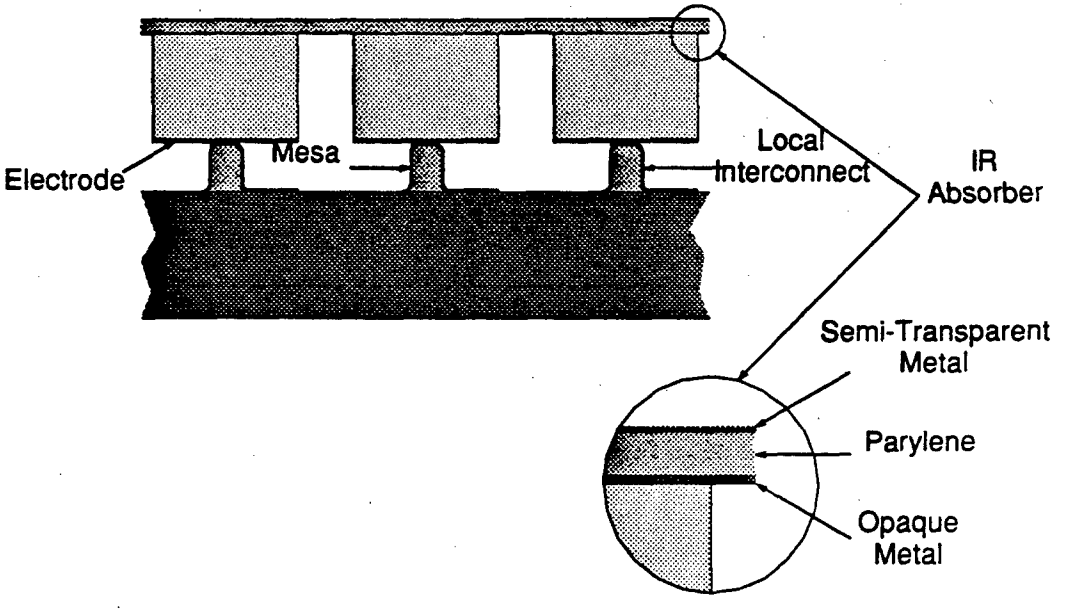

Figure 2 - Schematic drawing of uncooled detector pixel structure.

Both digital and analog outputs are present. This feature provides maximum compatibility with standard video equipment, including monitors and VCRs, and with computer hardware and software. It also permits taking advantage of commercially available image processing software for image enhancement and for diagnostic purposes. Although application specific software for medical diagnosis using thermal imaging is not generally available, if at all, there is an abundance of similar software and related expertise in both the medical community and the industrial community. Technology and even ready-made software already exists for important functions such as pattern recognition, spatial filtering, spatial and temporal analysis, and multi-frame integration and differentiation.

System size, weight and performance depend largely upon the IR optics configuration. Parameters typical of an uncooled thermal imaging sight operating at 30 frames per second are as follows:

Parameter	Value	Units
IR Lens Diameter	4.0	inches
IR Lens Focal Length	4.0	inches
System Weight	4.5	pounds
Power Dissipation	6.0	Watts
Angular Resolution	0.48	mrad
NETD - Specification	0.12	°C
Best	0.05	°C
Typical	0.08	°C

In configuring a system for a particular application, there are tradeoffs between sensitivity and resolution and cost, as shown in Figure 3. The extent to which the tradeoffs are available is limited by practical considerations in the IR optics design. The curves show only physically realizable designs. A further tradeofff exists between sensitivity and temporal response. By summing consecutive video frames the signal-to-noise ratio is improved at the expense of temporal information. The NETD is improved by approximately the square root of the number of frames summed.

Introductory prices will be in the range of $5,000 to $25,000 depending upon specifications, IR optics size, and ancillary equipment. Products of unusually high volume should eventually achieve even lower selling prices.

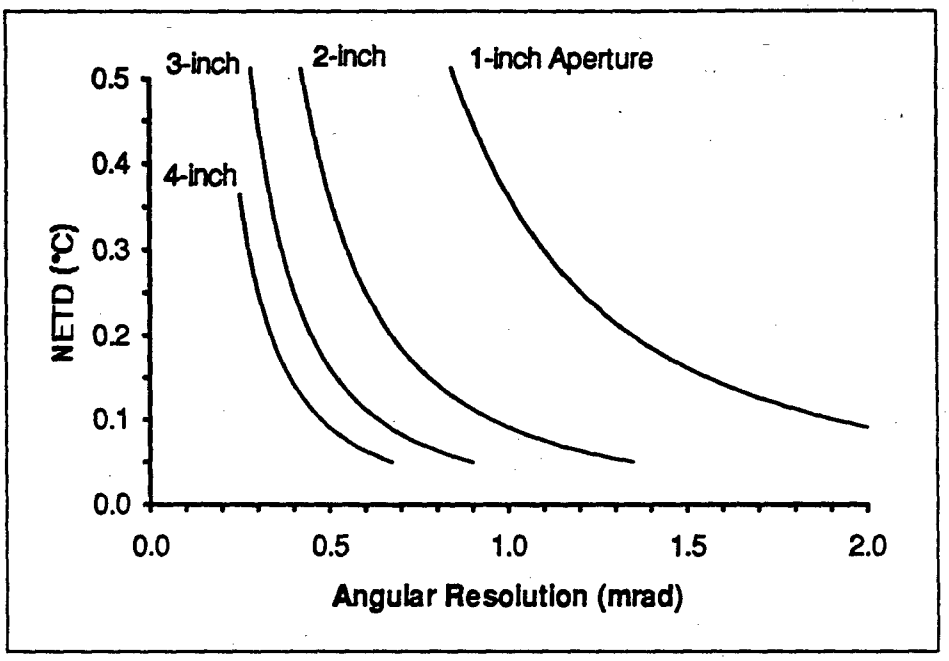

Figure 3 - Tradeoffs of sensitivity and resolution for a typical uncooled thermal imaging systems.

Applicability to Medical Uses

Thermal imaging is useful for medical diagnosis whenever superficial temperature variation, either spatial or temporal, is indicative of underlying medical problems. Physiological dysfunction as well as anatomical dysfunction can contribute to local abnormal thermal behavior. Dissipation of heat generated in the body is affected factors such as infection, mechanical integrity, blood flow, hydration and perspiration. These factors are of course complicated by body responses, normal and abnormal, such as thermoregulation, metabolism, and vascularization. Thus superficial temperature variations can bear a wealth of information concerning a variety of functions and dysfunctions.

The fundamental problem is to understand the relationship between observed thermal behavior and antecendent disorders. In certain cases (*e.g.*, breast cancer) links seem well established. In many other cases reactions between the problem and body responses to the problem sufficiently complicate the thermal profile to render it useless without significant research. Thermal imaging can be both the tool of the researcher and the tool of the practitioner. Only after research has clarified these issues can thermal imaging be applied for routine diagnosis. Although uncooled thermal imaging appears well suited to many thermographic applications, the market is not likely to develop until firm cause and effect relationships are established between disease of dysfunction and thermal profile.

Status and Plans

Several uncooled long-wavelength infrared system configurations are currently available or in development. Three militarized systems are in the late stages of development. A small arms weapon sight is the lightest weight, lowest power dissipation thermal sight currently available anywhere. A larger similar sight provides higher resolution for surveillance of distant scenes. A night driving aid improves the mobility of military vehicles. A commercial system is currently for sale with deliveries beginning the end of this year. It is a sensor that mounts behind the light bar of a police cruiser and provides remote control and a video display inside the car.

Detector arrays are presently in production at a rate of about 100 deliveries per month, and that rate will increase sharply over the next year. Performance is at a satisfactory level for the near future, but as production rates rise to fill the demand new applications will surely arise to demand better performance.

Other commercial thermal imaging systems planned for the near future are site surveillance systems and night driving aids for the trucking industry. Medical applications represent a new front of unknown potential. As the exchange of information among health care providers, medical researchers, patients and equipment developers increases, the relevance of the capabilities of uncooled thermal imaging technology will surely become apparent.

ROCKWELL'S LOW-COST HIGH-RESOLUTION INFRARED SENSORS MAKE INFRARED IMAGING AVAILABLE TO THE MEDICAL COMMUNITY

AUTHORS- GILPIN, JAMES B. and BELL, JAMES E.
ELECTRO-OPTICAL CENTER
ROCKWELL INTERNATIONAL
3370 MIRALOMA AVE.
ANAHEIM, CA. 92803

ABSTRACT-INFRARED FOCAL PLANE ARRAYS (FPAS), CONTAINING MORE THAN 65,000 INFRARED ELEMENTS, ARE BEING MANUFACTURED FOR COMMERCIAL SALE AT PRICES BELOW $10,000. THEY ARE IMMEDIATELY AVAILABLE AND ARE BEING INTEGRATED INTO INFRARED CAMERAS BY SEVERAL MANUFACTURERS. THESE CAMERAS ARE ALLOWING RAPID EXPANSION OF THE USE OF INFRARED IMAGING. THE TV- QUALITY RESOLUTION AND TEMPERATURE SENSITIVITY ENHANCE MEDICAL, INDUSTRIAL AND COMMERCIAL CAPABILITIES AS THE EXPERTS IN THEIR FIELDS TAKE ADVANTAGE OF THE ABILITY TO "SEE" THERMAL PROFILES IN PEOPLE, INDUSTRIAL PROCESSES, ENVIRONMENTAL POLLUTION AND MANY OTHER POSSIBLE USES. THE PAPER REFERENCES SOME POTENTIAL MEDICAL APPLICATIONS. IT DESCRIBES HOW THE FPAS ARE PRODUCED, HOW THE LOW COSTS ARE ACHIEVED AND SHOWS ACTUAL VIDEO FOOTAGE OF INFRARED IMAGING IN SEVERAL APPLICATIONS.

KEY WORDS: FOCAL PLANE ARRAYS, FPA, INFRARED IMAGING, THERMAL IMAGING, THERMOGRAPHY

INTRODUCTION

Rockwell has been a supplier of high-performance infrared (IR) Focal Plane Arrays (FPAs), primarily for military applications, for over a decade. The photo-sensitive material is mercury-cadmium-telluride (HgCdTe or MCT) manufactured into two-dimensional arrays for high-resolution imaging. The low-cost detectors are sensitive to 3-5 micrometer infrared radiation, commonly referred to as MWIR (medium wavelength infrared), making them ideal for sensing the self emission from the world around us. All objects emit infrared "light" which varies due to slight differences in temperature, shape, surface texture, material, and other factors. The resulting thermal profiles, which are characteristic of the object or region of interest, can be viewed with a passive system (without any external radiation or chemicals). Consequently, thermal images can be observed by utilizing FPAs to provide television displays with great detail. Such images can aid medical science by providing the doctor or researcher views beyond the visible, and complementary to those provided by other diagnostic and monitoring "tools." Just as color views of objects add insight into details not seen in black and white, infrared exposes even more information. Over the past few years, FPA manufacturers have made major advances in the sensitivity, reliability, size, and producibility of detector arrays. Until recently, high- resolution arrays (1/4 square-inch chips, with over 65,000 infrared elements each) cost more than $50K (not including the other parts used to make an IR camera), making this technology too costly for all but military applications. Rockwell's breakthroughs in large-area starting materials, manufacturing efficiencies and yields, have resulted in FPA costs of less than $8K. These 256 x 256 "staring" arrays are being purchased in quantity by several IR camera manufacturers, who are making their cameras available (at correspondingly low cost) for a wide range of civilian uses.

COMPONENT DESCRIPTION

Infrared cameras are much like the familiar video cameras many of us have in our homes. The charge-coupled device (CCD) chip, in the video camera, is replaced with an infrared FPA as shown in Figure 1. The FPA, shown in Figure 2, consists of two chips, the detector chip containing a 256 x 256 or larger array of detectors, and an integrated circuit chip (multiplexer) with an input amplifier for each detector element. They are bonded together with metallic indium "bumps"—one between each detector output and its corresponding amplifier input. Indium is a very soft metal (like solder) that cold welds when pressure is applied, thereby making both electrical and mechanical connections in one operation. The FPA is mounted in a small evacuated Dewar where it can be cooled to its optimum operating temperature. Control electronics and an analog-to-digital converter are added to make a "sensor-engine" module (Figure 3). This unit contains all the detector elements and the necessary electronics to produce a high-resolution thermographic image using standard video electronics and displays. The high-resolution infrared imagery, provided by large high-performance IRFPAs, offers major benefits to medicine, law enforcement, environmental monitoring, industrial process-control, and an exploding variety of other applications. Figure 4 illustrates some potential uses—drivers' vision enhancement, aircraft landing aids, security and law-enforcement, and medical thermography.

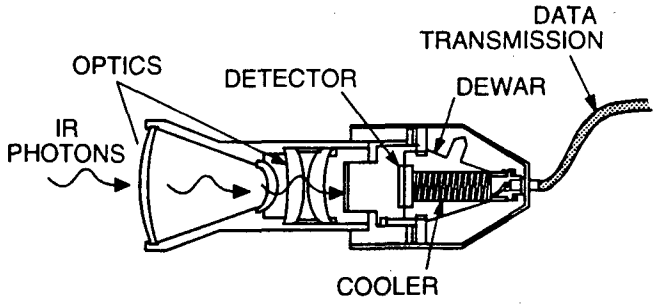

Figure 1. Infrared Camera

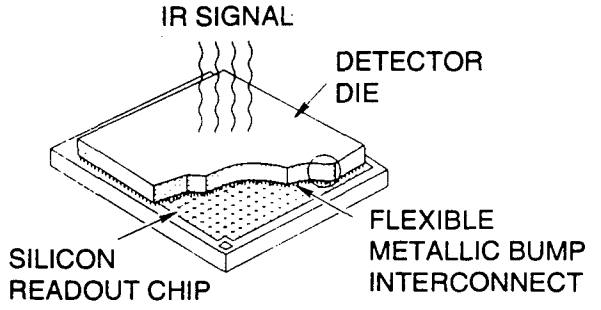

Figure 2. Infrared Focal-Plane Array (FPA)

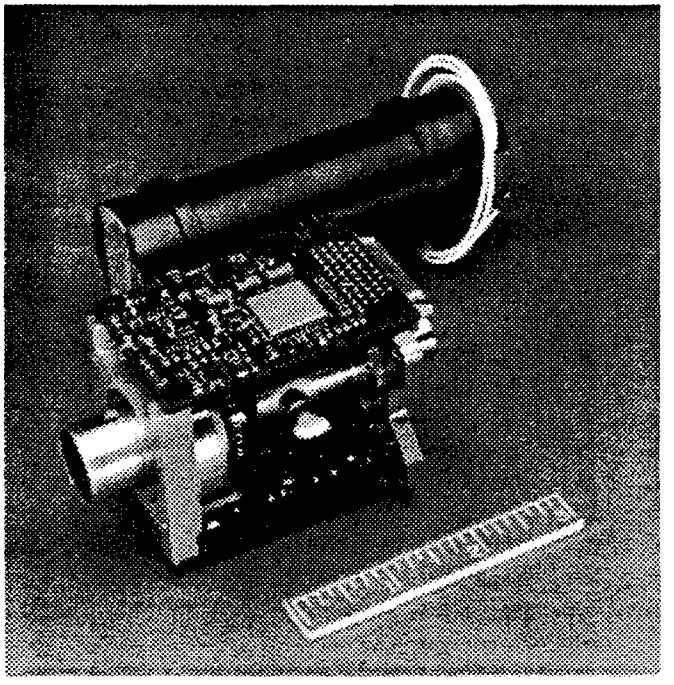

Figure 3. Sensor Engine and Continuous-Type Cooler

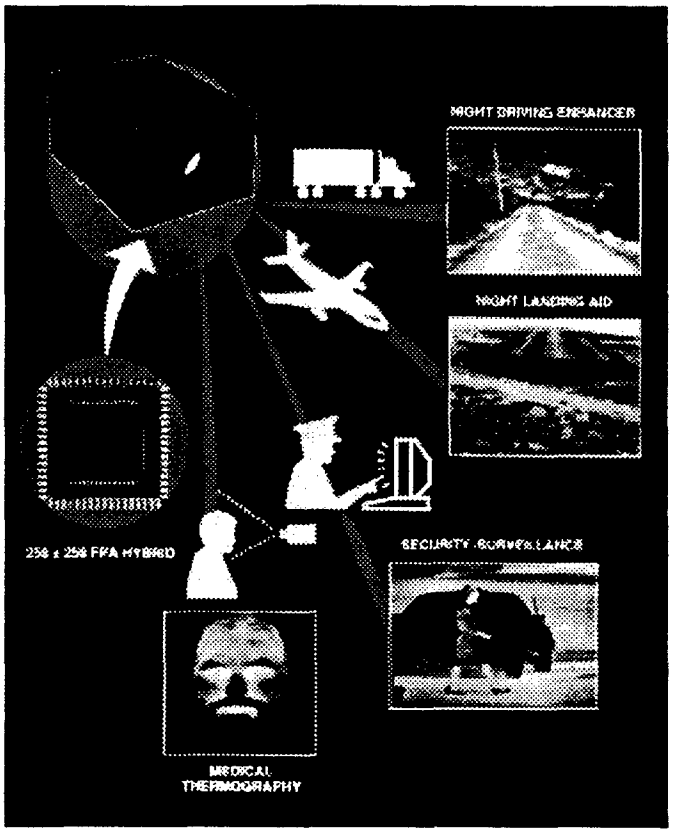

Figure 4 . Commercial Products

MEDICAL THERMOGRAPHY [1] [2]

Early (1970s through the mid-1980s) evaluations of infrared devices for thermography generally indicated inadequacies (e.g., poor sensitivity or resolution, non-uniformities, stability, reliability). These deficiencies were overcome, in the 1980s, as a result of government- and industry-developed technology and manufacturing methods. Devices are now capable of detecting temperature differences or changes of 0.01C, and "staring" arrays (where all the IR elements continuously observe the imaged region) are available with over a million elements. Figure 5 shows some photos taken of a television display of medical thermographic images. The actual images (versus these small photos) are higher resolution; nevertheless, even the photos indicate the potential utility of thermography now available for medical diagnostics and/or monitoring. The report of Reference [1] indicates a wide variety of potential thermographic applications, including imaging of

- Metabolic rates (normal, feverish)
- Perfusion (overabundance of blood flow) at skin level, reflecting supply to other regions well below the surface
- Neurological control of blood flow, reflecting functioning of the nervous system (and possibly

indicating, through blood-circulation monitoring, nerve-problems which result in back or other pain)
- Inflammation (including that associated with arthritis, rheumatism and even carpal-tunnel syndrome)
- Tumors
- Vascular disorders
- Migraine headaches
- Skin grafts, burned regions, skin disorders and cancers
- Cornea temperature, reflecting possible inner-eye disorders
- Blood and other liquid flow, and monitoring of organ temperatures, during surgery

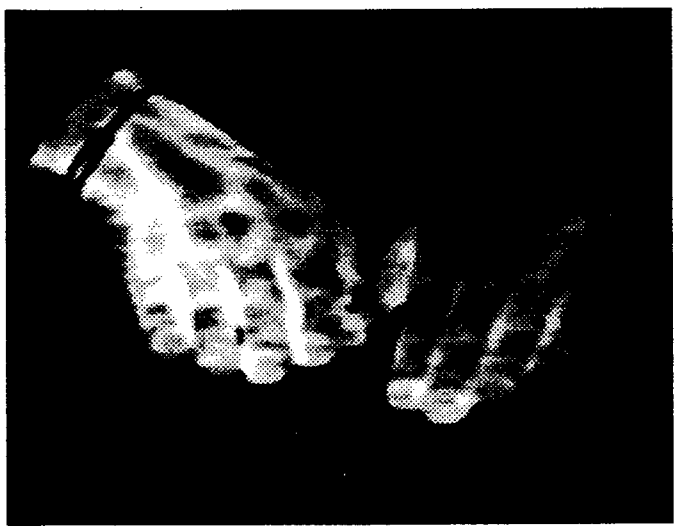

Figure 5a. Hands with Dissimilar Blood Flow

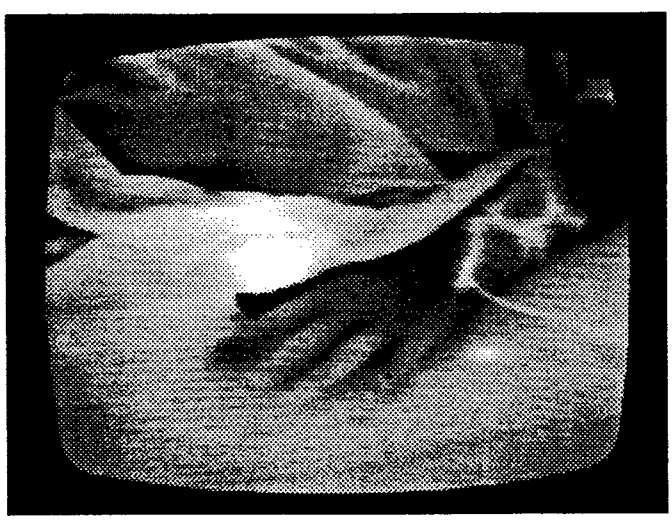

Figure 5b. Hand with Catheter and Fluid Entering Veins

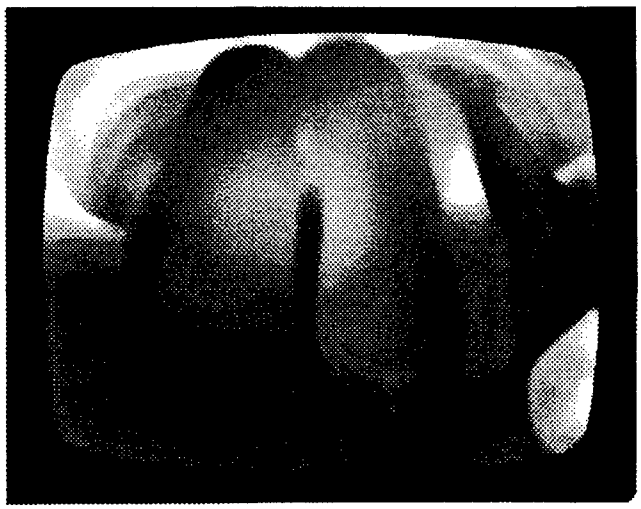

Figure 5c. Feet–One with Restricted Blood Flow

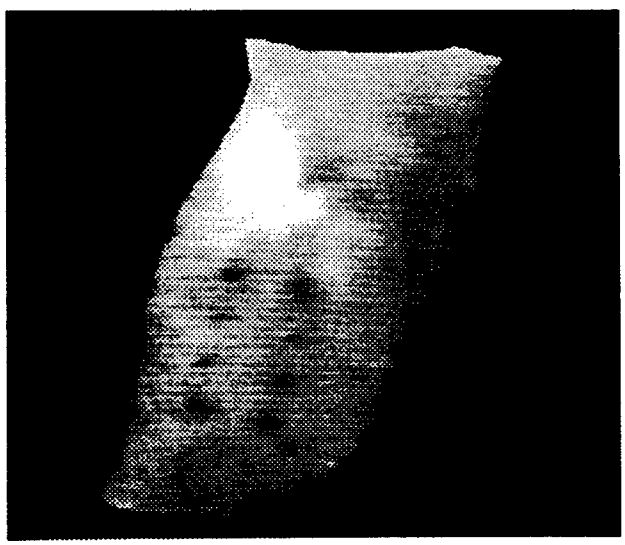

Figure 5d. Needle Marks Not Visibly Obvious

As might be deduced from the photos and the potential applications, thermography is generally an indicator of function, rather than structure, of the imaged region. (E.g., x-ray mammography images potentially cancerous structures under the skin, whereas infrared thermography indicates metabolic rate due to inflammation or to dilation of veins within the breast.) Thermography can indicate abnormal heat-profiles, even when no structural changes can be observed by CAT (Computer-Aided Tomography) scanning or MRI (Magnetic-Resonance Imaging). Therefore, IR thermography is truly a unique complement to the diagnostic and monitoring tools already used by the medical community. After large, reliable, high-sensitivity IRFPA devices became available, and numerous applications of thermography were demonstrated, the only real obstacle to the commercial use of IR devices going into the 1990s, was cost.

LOW COST MANUFACTURING

Early high costs were caused by low yields, small starting-material and batch sizes, and extensive use of hands-on labor. Rockwell's manufacturing processes, shown pictorially in Figure 6, have been refined to achieve high yields (typically greater than 20% from starting material through tested and delivered parts). Large three-inch diameter wafers are processed, using batch processing to minimize costs. Extensive process and test automation (including automated cryogenic testing) have been incorporated to reduce labor costs. The use of large-area starting material, combined with automated batch-processing and highly efficient testing allows Rockwell's Electro-Optical Center to offer high-performance 256 x 256 IRFPAs for under $10,000 in a quantity of one. In large quantities, the offering price is even lower.

IR camera manufacturers, as well as other commercial and military users, are designing products and systems around the "low-cost" generation of infrared focal-planes. The medical community, also, will soon benefit from these advances, as it adds medical infrared thermography to its "arsenal" of diagnostic and monitoring techniques.

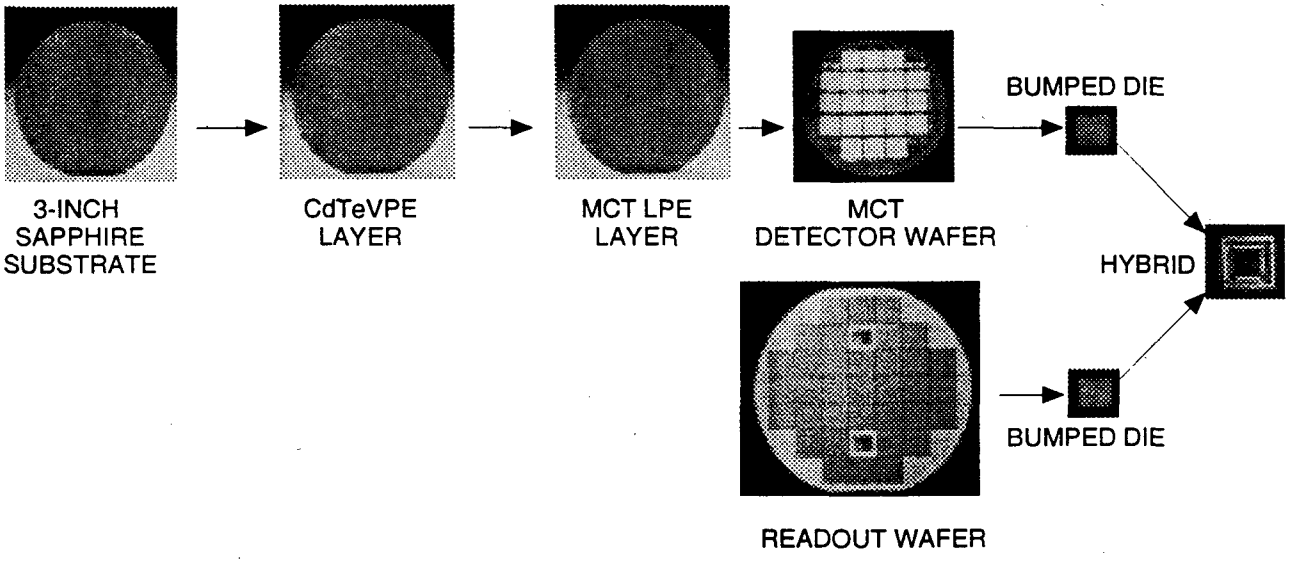

Figure 6. FPA Product Flow

[1] Dual-Use Applications Of Infrared-Sensitive Materials, Blechman and Lush, Defense Forecasts, Inc., June 1993.
[2] Private communication with Dr. Jagmohan Bajaj, Rockwell Science Center, October 1994.

PRE- AND POSTOPERATIVE DIGITAL INFRARED THERMOGRAPHIC IMAGING(DITI) OF THORACIC SYMPATHECTOMY FOR PALMAR HYPERHIDROSIS

Young-Soo Kim, M.D., D.M.Sc., Yong-Eun Cho, M.D.

Spine center, Department of Neurosurgery, Yongdong Severance Hospital,
Yonsei University College of Medicine, Seoul, Korea

Abstract

Essential palmar hyperhidrosis is a diseases characterized by excessive sweating on palms and hands due to hyperaction of sympathetic nervous discharge. It develops severe hypothermia on both hands because of loss of surface heat by evaporation of the heating. The sweating status has been detected by starch-iodine test, which is complicated and looks very dirty.

Recently Digital Infrared Thermographic Imaging(DITI) is developed and it can show any thermal difference very clearly. We have used DITI not only for the diagnosis, bur for the operative follow up of the disease since 1990.

Bilateral upper thoracic (T2 & T3) sympathetic ganglionectomy were performed in 199 cases between 1989 and 1994. Among them, open surgeries with posterior midline approaches were initially carried out in 54 cases and recently percutaneous endoscopic sympathectomy in 145 cases.

Pre- and postoperative thermal changes were analyzed in 527 DITIs. Preoperatively severe hypothermia is noted in 96.1 % in both hands and foot. Hyperthermic pattern is revealed in 5.9 cases. Immediately after operation the sweating is ceased in all cases and marked hyperthermia is noted is noted in both hands compared to preoperative status due to denervation hyperthermia. Postoperative compensatory hyperhidrosis was developed om the trunk below the level of sympathectomy in 38 cases(19.1%) which showed marked hypothermia on DITI.

Digital Infrared Thermographic Imaging technique is a simple and definite diagnostic method for hyperhidrosis and very useful for postoperative clinical monitoring.

Introduction

Essential palmar hyperhidrosis is a sudomotor dysfunction of sympathetic nervous system and causes severe difficulties during daily living due to excessive sweating from both hands. Sweat glands of the body are composed byeccrine glands and apocrine gland and it is innervated by cholinergic fiber. When the fibers are activated, it causes vasodilatation and sweating from the body.

Thoracic sympathectomy is a definite treatment for palmar hyperhidrosis. There was no exact method to detect autonomic dysfuction especially temperature changes of body. Recently digital infrared thermographic imaging technique, so called DITI is developed and it can show any thermal differences in the bosy clearly. It can detect dysfuction of autonomic nervous system exactly.

Authors performed total 199 cases of thoracic sympathectomy for palmar hyperhidrosis and evaluated pre- and postoperative thermographic findings by digital infrared thermographic imaging techniques.

Materials & Methods

We evaluated 451 patients who had eacessive sweating from palms and hands and diagnosed as essential palmar hyperhidrosis in spine center, Yongdong Severance Hospital, Yonsei university College of Medicine, Seoul, Korea since 1990. They took digital infrared thermographic imagings with DITI apparatus (DOREX®, DOREX Inc, USA). Among them 199 patients took thoracic sympathectomy at the second and third thoracic ganglions by open surgeries or thoracoscopic sympathectomy. We repeated DITI 7 days after surgery with same condition.

Digital infrared thermographic imaging examined in the room with 22°C temperature and constant air flow, humidity after adaptation to surrouding condition for 15minutes.

DITI was performed in pre-sweating state and sweating state in same patient as possible and the temperatures of palms, dorsum of hand and trunk were measured. The

thermal patterns of the patients were analyzed preoperatively. The thermal differences(ΔT) of palms and dorsum of hands compared to trunk were measured in 14 patients of normal group and patient group. Postoperative DITI were evaluated with same method and compared to preoperative fingings. Delayed DITIs were performed in some cases.

Results

1. Thermographic patterns

From April, 1990 to September 1994, total 527 cases of DITI examinations were performed in 439 patients. of hyperhidrosis. Initial thermographic findings were analyzed and thermographic patterns were classified into hypothermic pattern and pyperthermic pattern. Hypothermic pattern revealed abnormal severe cold areas on both palms and dorsum of hands compared to trunk(Figure 1). Hyperthermic pattern revealed warm or hot area on the palms and dorsum of hands inspite of excessive sweating(Figure 2). Hypothermic pattern appeared in 422 cases (96.1%) among 439 patients. Remained 17 cases(3.9%) showed hyperthermic pattern(Table 1)

Table 1. Thermographic patterns

Patterns	No. of cases	%
Hypothermia	422	96.1
Hyperthermia	17	3.9
Total	439	100.0

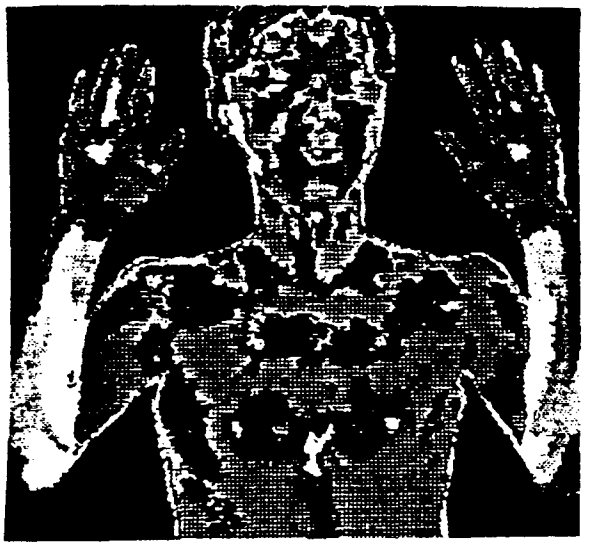

Figure 1. Hypothermic pattern. Severe cold area are noted in both palms.

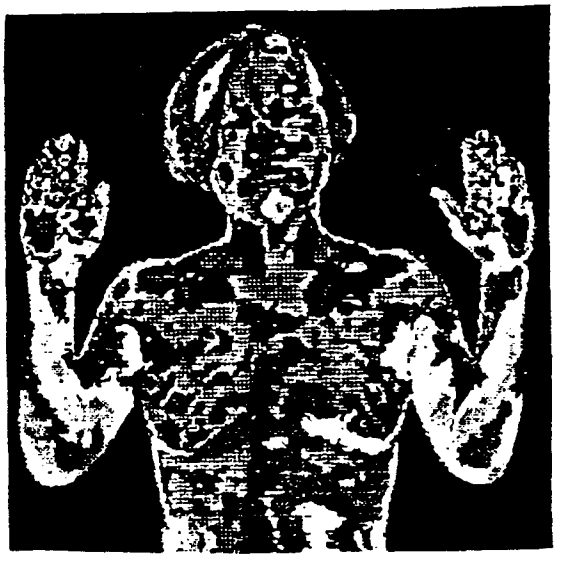

Figure 2. Hyperthermic pattern. hot areas are noted in both palms.

2.Thermal difference compared to trunk

In normal group(14 cases) and hypothermic patient group(422 cases), temperatures were measured in both palms, dorsum of hands and trunk and the thermal difference(ΔT, °C) in palms and dorsum of hands compared to trunk were analyzed. In normal group, ΔT was 0.2±0.1 °C in the palm and 0.3±0.1 °C in the dorsum of hand. In hypothermic group, they showed severe ΔT compared to noemal group($P<0.001$). The thermal differences were 2.9±0.6 °C in the palm and 2.4±0.4 °C in the dorsum of hand(Table 2).

Table 2. Thermal differences compared to trunk

Group	Sites	ΔT(°C)
Normal (N=14)	Palm	0.2 ± 0.1
	Dorsum of hand	0.3 ± 0.1
Hyperhidrosis (N=422)	Palm	2.9 ± 0.6
	Dorsum of hand	2.4 ± 0.4

3. Operations

Since March, 1989, 199 cases of thoracic sympathectomy were performed for palmar hyperhidrosis. In all cases bilateral second and third thoracic sympathetic ganglions were removed. Among them open surgeries with posterior midline approach were 54 cases and thracoscopic sympathectomy were 145 cases(72.9%).

Hyperhidrosis was more common in female than in male

(M:F=1:1.3) and most common in early twenties (Figure 3).

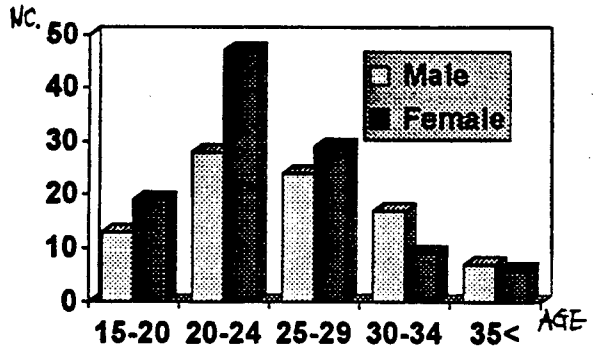

Figure 3. Age & sex distribution of operated patients

4. Result of operation

After surgery, excessive sweatin was completely cured in all cases. Postoperative transient minor sweatin was noted in 10 cases(5%). Recurrence was appeared in one case of thoracoscopic sympathectomy 7months after operation. Postoperative compensatory hyperhidrosis in trunk were developed in 38 cases (Figure 4). Minor complications were honor's syndrome (8 cases), neuralgia(7 cases), pleural effusion(1 case), transient atelectasis(4 cases), Pneumothorax(3 cases) and gustatory phenomenon(2 cases).

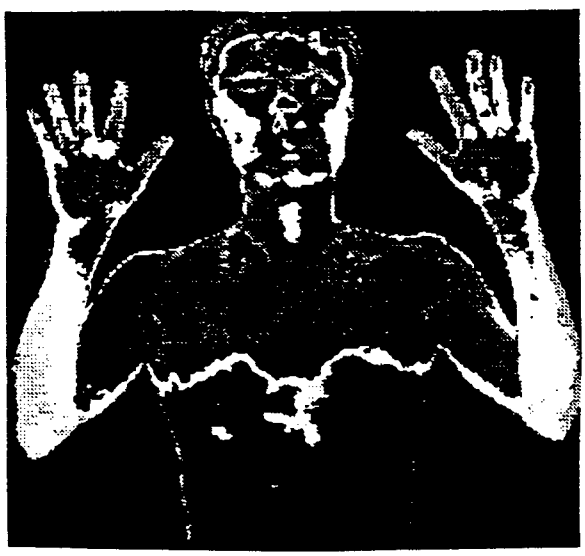

Figure 4. DITI finding of postoperative compensatory hyperhidrosis. Severe hypothermia is noted below T4 level.

5. Postoperative Thermographic findings

In 96 cases of operative patients, postoperative DITI eaxminations were performed. They all showed severe hyperthermia on palms and dorsum of hands compared to preoperative thermographic findings(Figure 5). Mean thermal differences(ΔT) were 3.1 ± 0.4 °C in palms and 0.5 °C in soles compared to preoperative state($P<0.001$).

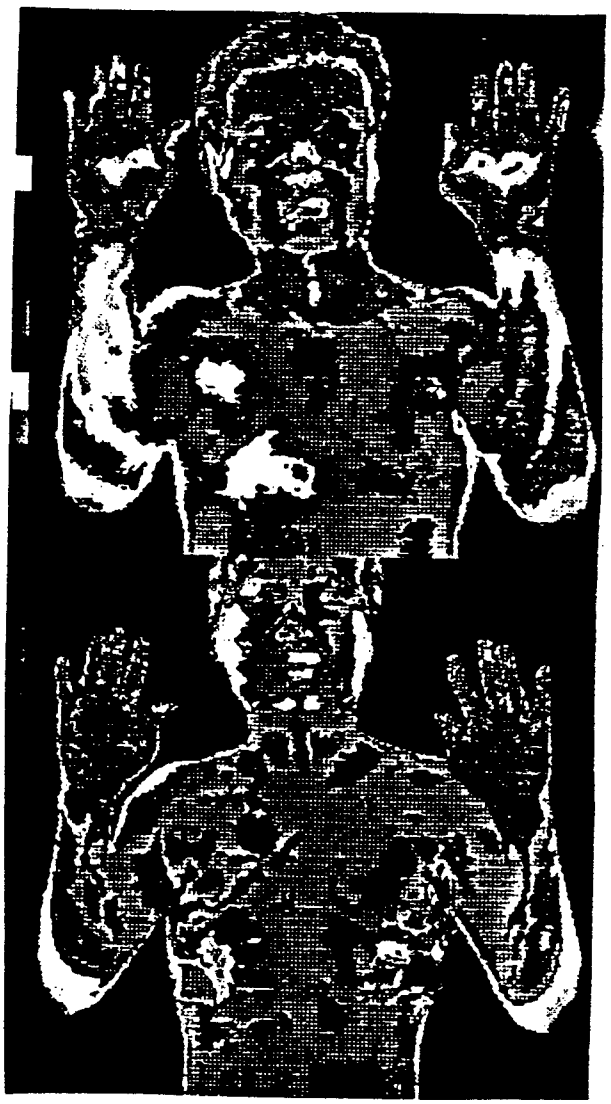

Figure 5. Preoperative(upper) and postoperative(lower) thermographic findings after sympathectomy. Preoperative cold areas are changed into hyperthermic areas.

Discussion

Palmar hyperhidrosis is a disease characterized excessive sweating on both hands and palmsdue to sudomotor dysfunction in autonomic nervous system.

Sweat glands in palms are innervated by cholinergic fibers of sympathetic nervous system and controlled by postganglionic fibers from the second and third thoracic sympathetic ganglion[1)3)]. When the postganglionic cholinergic fibers are activated, it causes a vasodilatation and sweating. In essential palmar hyperhidrosis, excessive sweating on both hands is due to hyperactivation of sympathetic nervous discharge and it causes severe coldness on both hands because of loss of surface heat by evaporation. So the second and third thoracic sympathectomy play a key role for treatment of palmar hyperhidrosis[2)].

There are many methods to detect the sweating status of the body. Starch-iodine test has been used for detection of sweating[2)]. The white colored starch was changed into dark color after chemical reaction with sweat. But it is very complicated and looks like dirty. Also this method makes some discomforts to patient.

Thermography can measure body temperature and evaluate physiological autonomic function of body by measuring the subcutaneous capillary blood flow[2)4)]. It is the only diagnostic tool for diagnosis of autonomic nervous dysfunction objectively. Recently digital infrared thermogtic examination is developed and it can measure the physiologic changes more accurately and objectively without any hazards and discomforts.[2)]

We used digital infrared thermographic imaging technique (DITI) for diagnosis of hyperhidrosis and postoperative follow up.

Almost of patients showed severe coldness on both hands which is caused heat loss by evaporation of sweat. The mean thermal difference was 2.9°C ± 0.6°C compared to trunk. 3.9% of patients showed hyperthermia on palms and hands inspite of excessice sweating. The possible mechanism of hyperthermia is suggestedas as follows: In initial stage of sweating, hyperemia on palm is started by vasodilatation due to activation of sympathetic cholinergic fibers[1)3)]. At that time, thermographic imaging shows hyperthermic pattern. As the sweating is more severe, the hand is coated with sweating and cooled by loss of heat due to evaporation. Then thermography revealed severe hypothermia.

We operated 199 cases of hyperhidrosis from March, 1899 to September 1994. Among them we performed 4 cases of starch-iodine test and 195 cases of digital infrared thermographic imaging(DOREX Inc, U.S.A.). The disgnostic accuracy of thermograpgy was 100%. It can evaluate exact body temperature and sudomotor dysfunction. It can be used for diagnosis of hyperhidrosis and autonomic nervous system disorders.

Postoperatively all patients cured excessive sweating immediately. There was no sweating from hands and palms due to sympathetic denervation. Postoperative DITI showed severe hyperthermia of palms and hamds caused by denervation hyperthermia. Comparing to preoperative state temperature elevation of 3.1±0.4°C is developed as a result of T2 & T3 sympathetomy. One case of recurrence is can be detected by thermography. In compensatory hyperhidrosis, DITI reveals severe hyperthermia on both arms and hands and above T4 level as a result sympathectomy. But marked hypothermia is noted in trumk and legs below T4 level. So it is useful for follow up of postoperative courses.

Conclusion

Digital infrared thermographic imaging is very useful for diagnosis of sudomotor dysfunction in autonomic nervous system. It can measure skin temperature changes accurately and objectively. Postoperative clinical courses also can be evaluated by thermography. Digital infrared thermographic imaging technique is a good diagnostic tool for hyperhidrosis.

References

1)Gross D: Pain and autonomic nervous system: Advances in neurology vol 4. New York, Raven Press, 1974, p93

2)Kim YS, Yoon DH:Thoracic Sympathectomy for Essential Hyperhidrosis. Journal of Korean Neurosurgical Society,22(1) 3-11, 1993.

3)Sato A,Schmidt RF: Somatosympathetic reflexes: Afferent fiber, General pathways, Discharge characteristics. Physiological Reviws 53(4)916-947, 1973

4)Uematsu S: Thermography: Neurological surgery. Edited by Yoomans. Saunders, 1990,p500